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THE USE OF COLPOSCOPY IN THE EARLY DETECTION OF CARCINOMA OF THE CERVIX.

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FOR a period varying from months to many years, carcinoma of the cervix remains in a preclinical phase. At this time it is usually symptomless and the clinical appearance is that of a normal cervix or an innocent erosion. Histologically it may be in a preinvasive or early invasive stage. The importance of its detection at this stage is that eradication means almost certain cure. The recently developed methods of cytological examination of exfoliated cells (Papanicolaou smear) and colposcopy can unearth these early cancers. While the value of cytological examination has almost universal acceptance, the method of colposcopy has to date been greatly neglected in the English-speaking countries. Mestwerdt (1953), Antoine (1954), Navratil (1957, 1958), Limburg (1958) and many other Continental gynæcologists believe that the best results are to be obtained by the complementary use of these methods. If their universal use was possible, the mortality from carcinoma of the cervix would become negligible.

The colposcope is an instrument which gives a small-scale stereoscopic magnification of the cervix of 6, 10, 16 or 25 times. It represents a transition from macroscopic to microscopic vision, so that one can see mucous membrane changes not visible to the naked eye, and from these it is possible to forecast the actual histological findings with surprising accuracy. The colposcope was created in its primitive form by Hinselmann in Hamburg in 1925, but it took many years of laborious correlation with the histological findings before the new colposcopic appearances were fully understood and a new terminology was evolved. In 1928, Herbert Schlink, seeing its possibilities, brought one back to Sydney with him from Germany, but unfortunately little was understood about the method at the time. Today the instrument is vastly improved, and is widely used throughout Germany, Austria, Italy, Switzerland and France. It is also used in Egypt (Youssef, 1957) and South America (Salgado *et alii*, 1949). In the United States of America, Martzloff (1934) and Ries (1932) reported their experience with colposcopy at a time when the method was still in its infancy. The only recent report of its modern use in that country is from the Philadelphia school (Scheffey and

Lang, 1955, *a* and *b*). There have been no publications reporting its use in Great Britain.

While studying colposcopy abroad, I heard great surprise expressed many times that the method was not used in the English-speaking countries. There have probably been three main reasons for this delay in its adoption. The first has been language difficulties, the lack of scientific papers in English on the subject and the necessity of foreign travel to learn the technique. Secondly, the necessity of learning some new and unfamiliar terms may also have discouraged its use. Thirdly, there have been published comments by some eminent gynæcologists, such as the late Emil Novak (1955 and 1958), throwing doubt on the value of this instrument. Having now had experience with this method I am convinced of its great value, and I believe it is only a matter of time before it is used in all countries.

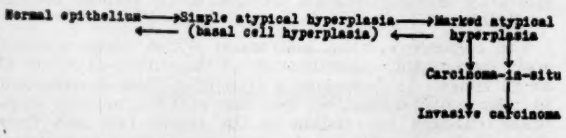
This paper outlines the technique of colposcopy and describes the more common colposcopic findings. The results of the first three years' experience with the instrument at King George V Hospital, Royal Prince Alfred Hospital, Sydney, and a discussion of the value of the method in the early diagnosis of carcinoma of the cervix are to be published elsewhere (Coppleson, 1959).

Pathogenesis of Carcinoma of the Cervix and its Relation to Prophylaxis and Early Diagnosis.

As colposcopy gives a clinical understanding of the cervix, previously possible only on histological examination, it is necessary to review briefly the significance of certain changes which may take place in the cervical epithelium. The opportunities for prophylaxis and early diagnosis may then be clearly seen.

There is much evidence to suggest that changes in the basal layers of the cervical epithelium are the early phases in the development of carcinoma-in-situ (preinvasive carcinoma, Stage O carcinoma), just as carcinoma-in-situ itself precedes invasive carcinoma. These changes have been named atypical epithelium, atypical hyperplasia, unquiet epithelium, anaplasia and basal-cell hyperplasia, but all apply to the same histological picture. They have no resemblance to the common and perfectly benign histological pictures of "chronic cervicitis", "cervical erosion", epidermization or squamous metaplasia. The degree of activity of this atypical epithelium may be slight and confined to the basal layers (Figures I and II), or marked when the atypical cells extend further towards the surface to approach the full thickness involvement of carcinoma-in-situ (Figures III and IV). The probability of subsequent malignant change increases with the degree of the atypical hyperplasia.

The probable pathogenesis of carcinoma of the cervix is as follows:



In many cases, changes have now been observed to progress from atypical hyperplasia to carcinoma-in-situ. Such reports include those of Wespi (1949), Younge *et alii* (1949), Limburg (1952), Mestwerdt (1953) and Galvin, Jones and Te Linde (1955). Furthermore, these changes may often be seen histologically lying next to those of carcinoma. On the other hand, there is no doubt that in many of these cases atypical hyperplasia does not progress to carcinoma, but either persists or undergoes regression. It would seem, therefore, that the stimulus to this hyperplasia is not always neoplastic, but may also be inflammatory or hormonal.

Carcinoma-in-situ (Stage O), before the advent of cytology and colposcopy, was usually recognized only on routine pathological examination of specimens removed at operation. Although this histological appearance was described by Kermauner and Schottländer in 1912, it was Schiller in 1927 who first believed it to be preinvasive carcinoma. This lesion represents the extreme degree of atypical hyperplasia, and is diagnosed only when the full thickness of epithelium is involved. While practically no one today questions this lesion as a precursor of invasive cancer, it is still debated whether in all cases it progresses to invasion. The best evidence on this problem has been presented by Petersen (1956) and Kottmeier (1957). Petersen followed 127 patients without treatment for three years, and 38 for a minimum of ten years. Obvious invasive carcinoma had developed in 11% at the end of three years, in 22% after five years and in 33% after nine years. Kottmeier in a similar study found that 15 of 31 untreated cases had become invasive. It is also highly probable that some other of these early small carcinomata had actually been excised completely by the repeated biopsies necessary to ensure that invasion had not developed. In other cases, too, it is possible that the patient dies of intercurrent disease before invasion takes place. Further evidence is given by Galvin, Jones and Te Linde (1952), who made a retrospective study of biopsies performed one to seventeen years before the patients appeared with clinical cancer. In 11 of 13 cases carcinoma-in-situ was present, in one other there was marked basal-cell hyperactivity, and in the other there was no epithelium in the biopsy specimen.

The all-important practical point is that a latent period exists during the progress of preclinical carcinoma (including preinvasive or Stage O carcinoma and early invasive lesions) to clinically evident cancer. There is also a similar interval during the earlier change from marked atypical hyperplasia to preclinical carcinoma. In both, the latent period can be short, but it is more often prolonged over many years. This is obviously the time when we must try to detect these lesions. Unfortunately this is impossible by the traditional methods of examination, as these lesions are usually symptomless and arouse no clinical suspicion. It will be seen, however, that colposcopy easily differentiates these groups from other benign cervical conditions, and thus gives a great opportunity for the detection and treatment of cancer of the cervix in its earliest stage. Further, by the detection of premalignant conditions for thorough treatment and careful follow-up investigation, the colposcope will play an important part in the prophylaxis of this disease. There is no doubt that much more will be achieved by this means in the battle against cervical cancer than by any refinement in present-day methods of treatment.

The Instrument and Technique of Colposcopy.

The colposcope used in this hospital has been the Zeiss model (Figure V). It gives a stereoscopic magnification associated with excellent illumination, is easily manipulated and, having a focal length of 20 cm., does not enter the vagina. The instrument consists of two components, the stand and the colposcope proper. On the base of the stand there is a foot switch by which the illumination may be turned on and off. In the base is a transformer, and running from it is a cable which connects the instrument to the mains. By means of two swinging arms joining the colposcope to the stand and other devices, the instrument is easily moved in any horizontal or vertical direction, and may be fixed at will by locking screws. Magnifications of 6, 10, 16, 25 or 40 times are possible, and may be changed without refocusing. The instrument is fitted with a red-free filter or "green light", which increases contrast and allows better examination of the blood vessels. There is also a special attachment with "Contax" camera and electronic flash so that cervical lesions may be photographically recorded in colour.

The examination usually takes about two to three minutes and is painless. The cervix is first exposed with a speculum. The colposcope is then swung into a position so that the objective is about 20 cm. from the cervix. Fine focusing is then performed by the special control. The oculars are then adjusted at the correct width for the observer, for stereoscopic and not monocular vision is necessary for adequate examination. A magnification of 6 or 10 times is sufficient and allows a large area around

the external os to be seen in the one field. For small suspicious areas, a magnification of 16 times may rarely be useful, while magnifications of 25 or 40 times are unnecessary. Mucus is gently removed from the cervix with a dry gauze swab, and if this has not already been done, smears are taken for examination by the Papanicolaou method. The cervix is then viewed with the colposcope, and again after the application of a gauze swab saturated with 3% aqueous acetic acid solution. The acetic acid helps soften the mucus, allowing its easier removal, and by causing the tissues to swell, greatly increases clarity. Often a diagnosis of the cervical lesion is impossible before the application of this solution. Its effect may be transient, and further soaking may be necessary. The cervix is then viewed with the green light, and the vascular structure is examined. Finally, the cervix is dried and then soaked with Schiller's iodine solution. Sufficient solution should be used to bathe the cervix completely. The solution is made up as follows: iodine 2 grammes, potassium iodide 4 grammes, distilled water to 300 ml.

If suspicious areas are seen on colposcopic examination, a cervical biopsy should be performed. If the area is extensive or most suggestive of carcinoma, the patient is admitted to hospital, a large wedge is taken with a scalpel and the cervix is repaired. With the colposcopic selection of target areas, the larger cone and ring biopsies are usually unnecessary. Occasionally, with minor atypical colposcopic changes or areas with uncharacteristic yet not unduly suspicious appearances, a punch biopsy is taken at the time of the examination. With a good instrument the procedure is painless, and bleeding is usually slight. If it is persistent, an intravaginal tampon is inserted for 24 hours. The punch biopsy should also be used frequently by those learning the art of colposcopy, for the correlation of the colposcopic and histological pictures is most instructive. Any patient with suspicious colposcopic findings, proved by biopsy not to be carcinoma, must return at intervals for further colposcopic and cytological examinations.

The use of the correct type of examination table (Figure V) is most important and greatly facilitates colposcopy. The table was recommended to us by Professor Navratil, of Graz, during his visit to Sydney in 1958. It allows maximum comfort for the patient, ease of access for the doctor and minimal wastage of time. The patient simply lies on the table, rests her legs on the special rests and is immediately ready for examination. A further refinement in technique is the use of flat-right-angled anterior and posterior vaginal specula. They give the best exposure of the cervix, and with proper manipulation, the anterior and posterior lips of the cervix can often be separated and the lower part of the endocervical canal inspected. Several different sizes should be available. The use of a form to record the findings saves time and is of particular value in large-scale screening. A diagram on this form, used with suitable abbreviations for different colposcopic findings, saves lengthy descriptions and gives a much clearer understanding of the exact position of any lesion. By the use of this table, and the help of an assistant (whether doctor, student or nurse) to hold the special retractors, a nurse to pass the swabs and sterilize instruments and the special form for recording the findings, it is possible to examine the cervices of 15 or more patients per hour with the colposcope.

Colposcopic Findings.

It will be shown that the all-embracing term "cervical erosion" is a bad one, as it actually applies to at least eight entirely different types of mucous membrane change, some of which are definitely innocent while others indicate the possibility of malignancy. All these conditions are usually indistinguishable macroscopically, but are easily differentiated by the colposcope. "Chronic cervicitis" is another poor term, used by some gynæcologists instead of cervical erosion to denote most lesions around the external os. Most of these "cervical infections" can be seen by the colposcope to be simple changes with associated mucus-secreting glands, but without any evidence of infection.

The most common colposcopic findings and their probable histological associations are shown in Figure VI, and will now be described. Two of these findings, ectopic-columnar epithelium and healing erosion (transformation zone), form about 85% of what is commonly termed and understood by cervical erosion. Once these have been seen with the colposcope, one can guarantee benign histological findings in all cases. Atypical healing erosion (atypical transformation zone), true erosion, leucoplakia, ground leucoplakia and mosaic structure are the colposcopic appearances which suggest the possibility of early carcinoma. Biopsies must always be taken from these areas, and in nearly all cases there will be either atypical hyperplasia of varying degree (some types of which, as was stated earlier, are premalignant conditions), or actual carcinoma, either *in situ* or invasive. Limburg (1954), from his vast colposcopic experience, estimates the probability that these various colposcopically abnormal areas will prove to be the site of actual cancer as 9·8%, 9·9%, 9·4%, 13·2% and 9·9% respectively.

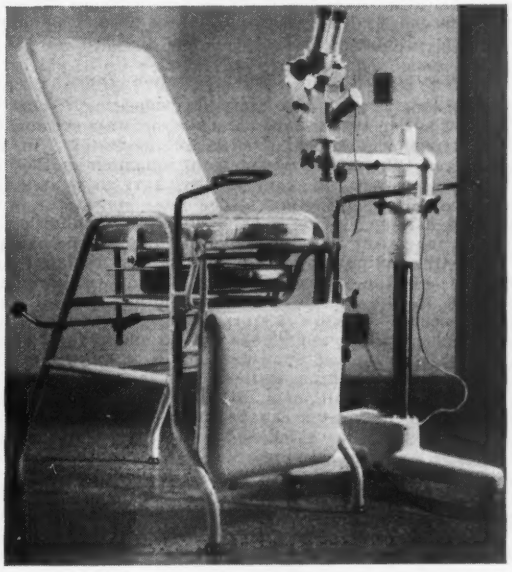


FIGURE V.
The colposcope and adjustable table.

Normal Squamous Epithelium.

The ectocervix or vaginal portion of the cervix is normally covered by squamous epithelium. With the colposcope it appears smooth and pale pink in colour. It meets the columnar epithelium and associated glands, lining the endocervix or cervical canal, at the squamo-columnar junction. This junction is usually situated at the margin of the external os.

Ectopic Columnar Epithelium.

Congenitally, or during or after pregnancy, or owing to an hormonal or inflammatory influence, the squamous epithelium around the external os undergoes maceration and is replaced by columnar epithelium from the cervical canal. This is known as ectopic columnar epithelium (*Ektopie*) (Figure VII). This epithelium has a typical grape-like appearance on colposcopic examination which is more easily seen after the application of the 3% acetic acid solution. Such an appearance is always benign. The area of ectopic columnar epithelium may be large or small, and may be present concentrically around the external os or only on one lip of the cervix. It is often covered by mucus from glands developing in this epithelium. Areas of ectopic columnar epithelium, to the naked eye, often

Macroscopic Appearance		Colposcopic Appearance	Histological Findings
Normal		Normal	Normal
"Chronic cervicitis" "Cervical erosion" (occasionally normal)	85%	Ectopic columnar epithelium	100% benign
		Healing erosion (transformation zone)	
		Atrophic cervicitis	
	15%	Atypical healing erosion	5%–10% carcinoma
		True erosion	
		Uncharacteristic red area	
		Mosaic structure	10% carcinoma and 80% atypical hyperplasia
		Ground leucoplakia	
Normal (occasionally leucoplakia)		Leucoplakia	
Carcinoma		Carcinoma	Carcinoma

FIGURE VI.

Colposcopic findings correlated with macroscopic and histological findings.

appear as most suspicious erosions. Post-coital and contact bleeding on vaginal examination may occur, as the columnar epithelium is fragile and easily damaged. Immediate clarification is possible with the colposcope. The typical grape-like epithelium is seen with the bleeding point to be merely a superficial lesion of normal columnar epithelium. Biopsy is never necessary in these cases.

Healing Erosion (Transformation Zone).

Spontaneously or after treatment, healing tends to occur. The change is known as a healing erosion or normal transformation zone (*Umwandlungzone*). In the early stages, thin vascular tongues of squamous epithelium can be seen growing in from the periphery to replace the ectopic columnar epithelium. The later stage of a well-developed healing erosion usually shows a combination of areas of ingrowing squamous epithelium, ectopic islands of grape-like columnar epithelium not yet replaced and the fate of the mucus-secreting glands which have developed in the ectopic columnar epithelium and have been preserved (Figure VIII). Some of these glands have been covered by squamous epithelium to form retention cysts, the largest of which are well known macroscopically as Nabothian follicles. The walls of these cysts appear as small, oval, whitish or yellow areas, in which prominent vessels can be seen. The white appearance is due to a thickened covering of squamous epithelium, and the presence of the vessels distinguishes the areas from leucoplakia. In other places the characteristic gland openings may be seen. Here, either the glands have escaped covering by the squamous epithelium, or intracystic tension has forced the gland open. These tiny open glands are seen surrounded by thin white rings of thickened squamous epithelium.

Occasionally complete healing takes place, with squamous epithelium replacing the whole area of ectopic columnar epithelium. In such a case the colposcope distinguishes this epithelium from the original squamous epithelium, by its slightly redder appearance, by the presence of more prominent vessels than usual in the underlying connective tissue, or by evidence of old mucus-secreting glands on the ectocervix. More often there is not complete healing, but a constant interplay of squamous and columnar epithelium over a long period. In most healing erosions, therefore, treatment by diathermy or cautery should not be delayed.

Healing erosions and ectopic columnar epithelium together account for most of the so-called cervical erosions. When these typical appearances are seen with the colposcope, biopsy is unnecessary, as the histological picture will always be benign.

Atypical Healing Erosion (Atypical Transformation Zone).

At times a healing erosion does not present the characteristic colposcopic picture described earlier. It must then be regarded with suspicion, for carcinoma may be present. In the interpretation of a healing erosion, the number, arrangement and calibre of the vessels seen by the green light are important. Normally they appear as fine branching capillaries in a symmetrical tree-like or radiating fashion extending along the tongues of ingrowing squamous epithelium. If the vessel course is disordered and the vessels have the atypical corkscrew shape mentioned later, biopsy must be performed. Suspicion should also be aroused when the ingrowing squamous epithelium is thicker and whiter than normal, approaching a leucoplakic appearance. In such cases it is often impossible to see the underlying vessels. The only thickenings of squamous epithelium in a healing erosion which should be considered normal are the white rings around the open glands and the epithelium covering the retention cysts. At other times the appearance can be even more atypical, and then it bears little or no resemblance to the typical healing erosion already described. The epithelium in such cases may be yellowish and glassy. Abnormal vessels are often associated.

Atypical healing erosion can be the most difficult of all epithelial changes to interpret by the colposcope. It is wise, therefore, to regard any variation from the typical changes, however slight, with suspicion, and to perform a cervical biopsy. If this is done, occasional cases of early carcinoma will not be missed.

Atrophic Cervicitis.

At the menopause or sometimes before it, the squamous epithelium becomes thinner and less vascular. The underlying vessels are easily damaged. Atrophic cervicitis is recognized colposcopically (Figure IX) by the pallor of the epithelium, which is usually associated with small subepithelial hæmorrhages. These hæmorrhages produce the reddened area on the cervix which explains many "cervical erosions" occurring in post-menopausal patients. The picture is characteristic and always benign. Biopsy need not be performed.

True Erosion.

In a true erosion (Figure X), the epithelium has been lost and the underlying connective tissue and its blood vessels can be seen with the colposcope. The importance of true erosion is that the denuded epithelium may have been fragile cancerous tissue.

Of great importance in the interpretation of a true erosion are the character of the blood vessels and the nature of the epithelium at the edge of the erosion. If, for example, one can see normal squamous epithelium or normal columnar epithelium adjoining a true erosion, and if the vessels are of the normal branching type, then it is most unlikely that malignancy exists. If, however, a true erosion is depressed below the level of the surrounding epithelium and lies amid an area of colposcopically atypical epithelium, such as leucoplakia, ground leucoplakia or mosaic, or if the blood vessels are of the corkscrew type, then the appearances must be regarded with great suspicion. In general, true erosions should always be subjected to biopsy.

Leucoplakia.

Leucoplakia of the cervix is a clinical term meaning white patch. The white appearance is due to a layer of keratin overlying the epithelium. When it is of sufficient size it can be recognized with the naked eye, but it can be

seen at a much earlier stage with the colposcope. It appears as a white, slightly elevated avascular and sharply demarcated zone (Figure XI). No vessels can be seen on examination with the green light of the colposcope. At first glance, adherent mucus may be mistaken for leucoplakia. If the superficial or cornified layers of the leucoplakic patch are wiped off, ground leucoplakia or, less commonly, mosaic structure will be seen. These colposcopically atypical forms of epithelium may also adjoin an area of leucoplakia.

It is essential that the purely clinical nature of this term be understood, for leucoplakia of the cervix implies no one histological picture. Areas of leucoplakia must always be examined by biopsy, and may show any number of conditions including simple atypical hyperplasia, marked atypical hyperplasia, carcinoma-in-situ and even invasive carcinoma.

Ground Leucoplakia.

Ground leucoplakia (*Grund*) represents a pattern of epithelial growth seen at a magnification short of the microscopic. It is a mucous membrane change which cannot be seen with the naked eye, but which is easily recognized by the colposcope. It shows as reddish dots set on a whitish-yellow background. Frequently it is at a deeper level and sharply demarcated from normal epithelium. The red dots correspond to fine capillaries in the points of papillary projections of epithelium. The coarser the projections ("papillary ground"), and the more atypical or corkscrew shaped the capillaries, the more likely is malignant change to be present. If an area of ground leukoplakia is covered by a cornified layer, it appears as leucoplakia. As this layer is easily lost and replaced, one can get the mistaken idea from macroscopic examination that leucoplakia is reversible.

All areas of ground leucoplakia must be examined by biopsy, and as with leucoplakia, histological examination will show either a non-malignant thickening of epithelium (atypical hyperplasia of varying degree) or actual carcinoma.

Mosaic Structure.

Mosaic (*Felderung*) is another atypical mucous membrane change invisible to the naked eye, but easily recognized by the colposcope (Figure XII). It appears as whitish-yellow fields separated by fine red lines. The separate areas are usually quadrilateral and may be large or small. Mosaic structure, like ground leucoplakia, represents another pattern of epithelial hyperplasia. The fields represent thick blocks of atypical epithelium, and the red lines are fine vascular connective tissue septa reaching to the surface between the blocks. At times there is a layer of keratin, so that these areas can at times appear as leucoplakia. All areas of mosaic structure must be examined by biopsy, and in nearly all, histological examination will show varying degrees of atypical hyperplasia or actual carcinoma.

Abnormal Vessels.

A clue to the possibility of cancer is given, not only by colposcopically atypical epithelium, but also by the appearance of abnormal vessels, the "corkscrew vessels", which are best seen under the green light of the colposcope. Normally the vessels have a typical tree-like or ray-like branching pattern. With the greatly increased blood requirements of malignant epithelium, the vessels undergo changes which can be recognized by the colposcope. The enormous vascularization which takes place is never so well shown in a histological section. At first the vessels become longer and broader and more numerous, but retain their form (adaptive vascular hypertrophy without deformity). With further development, the vessels lose their form and appear as typical short corkscrew-shaped vessels packed closely together. Eventually the blood supply cannot keep pace with the epithelial growth, so necrosis and ulceration set in.

The presence of the typical corkscrew vessels always indicates biopsy. However, they are not pathognomonic of cancer, as they may also be associated with atypical hyperplasias of the epithelium. The greatly increased vascularity in acute inflammation must be differentiated. Finally I must emphasize that corkscrew vessels are not seen in every case of carcinoma. I have seen, in a number of cases, well-developed carcinoma with only slightly broader vessels than normal.

Uncharacteristic Red Areas.

Sometimes a reddened area on the cervix is seen which resembles none of the colposcopic findings mentioned earlier. This area is usually covered by a very thin layer of squamous epithelium, and is hyperæmic, greatly increased vascularity being detected with the green light. At times this appearance may be difficult to distinguish from true erosion, and in fact the condition may prove to be a true erosion covered by an exudate. These areas are not seen often, but should always be regarded with suspicion. Biopsy usually shows an inflammatory process or true cervicitis, but on occasions the epithelium will prove to be the site of malignant change.

Iodine-Negative Areas.

The Schiller test should immediately follow the colposcopic examination, and in fact should be carried out as a routine in all pelvic examinations. The ectocervix and its surroundings are first dried and then extensively soaked with a gauze swab almost dripping with the solution. The excess liquid is then removed. The stain has usually completely disappeared by ten minutes.

Normally, squamous epithelium, containing glycogen, takes up the iodine and is stained a uniform dark brown or mahogany colour. There are, however, exceptions to this rule. The thin, newly formed squamous epithelium often uses up available glycogen and so remains unstained. Also, the squamous epithelium covering the cervices of some post-menopausal patients may give a speckled appearance, owing to the presence of small atrophic areas. Carcinoma, atypical hyperplasia and ectopic columnar epithelium, including those areas of columnar epithelium in a healing erosion, fail to take the stain. These abnormal or iodine-negative areas, however, present varying features. The areas may be white, yellow, pink or red, and the edges may be sharp or ill-defined and wavy. In general, all areas of a definite white or yellow colour, and all those with sharply limited boundaries, should be regarded with suspicion and always examined by biopsy. Iodine-negative areas with wavy and indefinite boundaries are usually benign. In the absence of the colposcope, which allows much further differentiation, it is safest to take biopsies from all iodine-negative areas which do not appear to be typical circular areas of ectopic columnar epithelium. These latter areas usually have an orange colour after staining.

The main advantage of the Schiller test, when it is used together with colposcopy, is to ensure that no atypical area has escaped close examination with the colposcope. On rare occasions, too, sharply limited iodine-negative areas are revealed which have shown no atypical features on colposcopic examination. These areas should always be examined by biopsy, although it is most unlikely that carcinoma will be found. Nearly all will show parakeratosis (imperfect keratinization) of the squamous epithelium.

Carcinoma.

The main use of the colposcope is to detect carcinoma in a cervix with no suspicious appearance on naked-eye examination. Cancer at this stage is suggested by the presence of one or more of the abnormal colposcopic findings already described. These include leucoplakia, ground leucoplakia, mosaic structure, true erosion, atypical healing erosion and the atypical corkscrew vessels. Biopsy of these areas will, as has been mentioned already, show carcinoma in a percentage of cases.

A later stage of carcinoma may show on colposcopic examination as a tiny ulcer, or as irregular glassy yellow areas of epithelium giving a characteristic "mountain range" appearance under stereoscopic vision. At the edge of these areas, other suspicious colposcopic appear-

ances or abnormal vessels are often seen. These are the earlier stages of the small ulcer or papillary overgrowth which are usually the first macroscopically detectable sign of cancer. All ulcers or any epithelium showing differences in level on colposcopic examination must be regarded with great suspicion.

Colposcopy is unnecessary in the case of clinically obvious cancer. Here the ulcer or cauliflower growth is already destroying the cervix. The findings in such cases are singularly uncharacteristic and are usually masked by superficial necrosis, discharge and hæmorrhage.

Discussion.

A colposcopy clinic was commenced at King George V Hospital, Sydney, in November, 1955, with the prime object of detecting preclinical carcinoma of the cervix. The method has been used together with cytological examination (the Papanicolaou smear method), which has been under the direction of Dr. Mary Heseltine. The number of in-patients and out-patients examined by these methods has been steadily increasing, and it is planned in the near future to "screen" all public patients attending the hospital.

This combined service has already had considerable success, and the results of the first three years' experience are reported in detail elsewhere (Coppleson, 1959). Most important has been the discovery in 11 cases of preclinical carcinoma of the cervix, appearing to the naked eye as a normal state of the cervix or an innocent erosion, and quite unrecognizable by the traditional methods of examination. Had a colposcopic and/or cytological examination not been performed, a cervical biopsy would not have been performed in any case. The methods by which these carcinomata were recognized were as follows: cytological examination (negative colposcopic findings in one case), four cases; colposcopic and cytological examination, three cases; colposcopic examination (negative cytological findings), four cases.

These results show that each method can fail, and indicate that the best results will be obtained by their complementary use. The value of this combination is surely obvious, even if one considers only the major deficiencies of each method. Cytology, for example, has a false-negative rate estimated by Navratil (1957), from a study of material from many clinics, at between 10% and 20%. Colposcopy, in competent hands, will detect most cases of early carcinoma on the ectocervix (portio vaginalis), but fails to detect endocervical carcinoma. Neither method, of course, replaces cervical biopsy for the final diagnosis.

The importance of colposcopy in the investigation and follow-up of patients with premalignant conditions of the cervix has already been mentioned earlier in this paper. The colposcope has several other advantages which are discussed elsewhere (Coppleson, 1959). These include the selection of the best site for cervical biopsy, which can be of value in both clinically suspicious and apparently benign appearances in the cervix. In many other cases it renders biopsy unnecessary. In the absence of colposcopy any cervix with contact bleeding should always be examined by biopsy. However, the colposcope shows many of these "bleeding erosions" to be benign lesions with no possibility of malignancy. This is of obvious value in pregnancy, and often saves the delay of a preliminary biopsy to exclude malignant disease before such procedures as total hysterectomy and pelvic floor repair.

Colposcopy is a great advance, not only in the early detection of carcinoma, but for a clinical understanding of cervical lesions in general. To be effective, however, the technique must be properly learned. The importance of this has been stressed by Hinselmann (1954), Mestwerdt (1953), Limburg (1952) and other writers. Antoine (1954) sums up these views when he states: "The instrument alone, not handled by an expert, is useless." It is essential that more and more gynæcologists, as in Europe, become trained in the use of the colposcope; but unless this competence is obtained, the method will fall into disrepute. The most important initial step in this country would seem to be the development of detection centres in all large gynæcological departments for large-scale screening of out-patients and in-patients, as well as all women who wish to have a cancer check. Such a scheme will be in operation at King George V Memorial Hospital, Sydney, from July, 1959, after the opening of the West Cancer Detection Centre for Women. All public gynæcological patients attending this hospital will then have cytological and colposcopic examinations. If it is ever possible for all women in the community to have these examinations at regular intervals, carcinoma of the cervix, instead of being the second greatest cancer killer in women, will have, even with present-day methods of treatment, a cure rate of nearly 100%.

Summary.

1. Colposcopy, a method giving a small-scale stereoscopic magnification of the cervix and of great value in the early detection of cervical carcinoma, has to date been greatly neglected in the English-speaking countries.

2. The relationship between atypical hyperplasia, carcinoma-in-situ and invasive carcinoma of the cervix is defined. The prospect of detecting carcinoma at a stage before the appearance of symptoms or obvious signs is mentioned.

3. The instrument and the technique of colposcopy are described.

4. The most common colposcope findings and the significance of each are described in detail. The colposcope shows that the terms "cervical erosion" and "chronic cervicitis" actually apply to at least eight different conditions.

5. The discovery of 11 cases of unsuspected carcinoma of the cervix by colposcopic and cytological examination at King George V Hospital, Sydney, is mentioned. The importance of the complementary use of these methods in the detection of preclinical carcinoma of the cervix is discussed.

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TRAUMATIC PNEUMOTHORAX.

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TRAUMATIC PNEUMOTHORAX can be dangerous to life. When associated with more obvious injuries, it may go unrecognized in its early stages.

The purpose of this paper is to review a series of five recent personal cases which occurred in a six-months' period. The mode of presentation, the treatment employed and the complications encountered are discussed.

Pathology.

When air enters the pleural cavity a pneumothorax results and the lung collapses, unless it is held in position by adhesions. A traumatic pneumothorax results from a perforating wound of the chest wall, or from a closed thoracic injury.

Despite the fact that the deflated lung serves no respiratory function and results in a venous-arterial shunt, a simple traumatic pneumothorax causes few symptoms in a healthy subject at rest. Symptoms depend on the extent of pulmonary collapse and mediastinal shift, and the more rapidly these occur, the more marked are the symptoms likely to be.

Complications of Traumatic Pneumothorax.

Tension pneumothorax develops when a valvular wound in the lung or chest wall permits a one-way escape of air into the pleural cavity. As the intrapleural pressure rises, the mediastinum is pushed to the opposite side, venous return to the heart is impeded and severe shock and dyspnœa ensue.

Hæmorrhage from intercostal vessels or fractured ribs after a traumatic pneumothorax results in the complication of hæmopneumothorax and its attendant danger of empyema. Bleeding from lacerations of the lung is rarely contributory, owing to the low pulmonary blood pressure (30/15 mm. of mercury).

A sucking pneumothorax can occur only after an open chest wound. To the disability of a collapsed lung is added the danger of mediastinal flap. During inspiration, air is sucked into the pleural cavity through the chest wound, and the mediastinum is pushed to the opposite side. Expiration results in a reversal of these effects, and the consequent movement of the mediastinum causes severe shock.

Reports of Cases.

CASE I.—A fit man, aged 32 years, was admitted to hospital on June 8, 1957, having been thrown from a horse. He had been unconscious for ten minutes and had vomited on recovery.

On examination his temperature was 97° F., his pulse rate 68 per minute and his respiration rate 18 per minute. His blood pressure was 120/75 mm. of mercury. His general condition was good, and there was good air entry into both lungs. The left clavicle and the upper left part of the chest were tender, but there was no clinical evidence of fracture.

X-ray examination of the left shoulder region on June 9 showed an undisplaced fracture through the neck of the first rib. There was no pneumothorax evident in this film.

Because of persistent pain, X-ray examination of the shoulder was repeated on June 11. No further fractures were found, but a left pneumothorax was evident. Confirmatory X-ray examination of the chest revealed a total left pneumothorax. There was no pleural effusion or mediastinal shift, but slight subcutaneous emphysema was present.

No specific treatment was instituted, as it was expected that the pneumothorax would rapidly absorb. The patient was discharged from hospital, symptom-free, five days after his admission.

On review 11 days after injury, signs of pneumothorax were still evident, and he was readmitted to hospital, where an X-ray examination of the chest revealed a 50% pneumothorax. Underwater drainage was instituted from a needle in the second left intercostal space.

The lung expanded within 24 hours and the needle was removed. At this time there was a small effusion in the left costophrenic angle. Follow-up examination two months after injury revealed no abnormal physical signs, and no abnormalities were found on X-ray examination of the chest.

The feature of this case was the delayed development of the pneumothorax, which gave rise to no symptoms. Had the shoulder not been radiologically examined, it is probable that the pneumothorax would have remained undiagnosed. The slow collapse of the lung must have resulted from a minute pulmonary leak, however caused.

CASE II.—A boy, aged 18 years, was admitted to hospital on October 12, 1957, having been involved in a motor cycle accident. Owing to a head injury he had amnesia for the event.

On examination his temperature was 97·8° F., his pulse rate 100 per minute and his respiration rate 22 per minute. His blood pressure was 125/75 mm. of mercury. The patient was conscious, but he had facial lacerations. An obvious right pneumothorax and moderate surgical emphysema of the thoracic wall were present.

X-ray examination revealed a 50% right pneumothorax with no shift, no pleural fluid, and moderate subcutaneous emphysema. There were non-displaced fractures of the posterior ends of the second, eighth, ninth and tenth right ribs.

The pneumothorax was needled in the second right intercostal space and an underwater drain attached. The lung reexpanded in 24 hours. At follow-up examination on December 30, the patient was fit and symptom free.

This was an uncomplicated case of traumatic pneumothorax, which responded rapidly to needling.

CASE III.—A man, aged 59 years, was admitted to hospital on October 16, 1957, having fallen 12 feet on to his head. He had been unconscious for an unknown length of time.

On examination his temperature was 98·8° F., his pulse rate 92 per minute and his respiration rate 18 per minute.

His blood pressure was 160/90 mm. of mercury. Severe facial lacerations were present. The right clavicle was fractured. Movement of the cervical and thoracic spines was painful. Air entry to the upper lobe of the right lung was poor.

X-ray examination revealed a 75% right pneumothorax with fracture of the second to the seventh right ribs distal to their necks. The fracture of the second rib was the most severe. There was no mediastinal shift or pleural effusion, and there was minimal subcutaneous emphysema. A fractured anterior cranial fossa was also revealed.

The pneumothorax was needled in the usual way. Penicillin and streptomycin were given. The needle was withdrawn after 24 hours, but 48 hours after injury a tension pneumothorax developed. This caused mediastinal shift and severe dyspnœa. Further needling immediately relieved the condition, and X-ray examination of the chest showed only a 25% pneumothorax. However, the pneumothorax gradually increased in size, necessitating further needling and bronchoscopic aspiration on two occasions.

Fifteen days after injury there was still a 20% pneumothorax with minimal fluid in the costophrenic sulcus. As the patient was symptom-free he was discharged from hospital.

X-ray examination of the chest at a follow-up investigation on November 13, showed a 15% pneumothorax with fluid still present. On December 18, the skiagram of the chest showed no abnormalities.

There was no difficulty in the clinical diagnosis of the pneumothorax in this case. The later development of a tension pneumothorax suggests a continuing valvular pulmonary leak into the pleural cavity. There must also have been an element of bronchial obstruction since, despite needling, reexpansion of the lung did not occur until bronchoscopic aspiration was performed.

CASE IV.—A woman, aged 45 years, was admitted to hospital on November 22, 1957, having injured the left side of her chest on a farm implement when trying to stop a runaway horse. She sustained an open thoracic wound, and during the journey into hospital she collapsed, her blood pressure falling to 80/55 mm. of mercury. A local practitioner sealed the wound and gave her a quarter of a grain of morphine.

On examination her temperature was 98° F., her pulse rate 92 per minute and her respiration rate 32 per minute. Her blood pressure was 105/75 mm. of mercury. The patient was apprehensive and gasping for breath. There was a linear sutured wound three inches long in the line of the eighth left rib in the mid-lateral position. Obvious surgical emphysema was present round this wound. A left pneumothorax was clinically evident. The only associated injury was a lacerated left forearm.

X-ray examination showed a 50% pneumothorax with some fluid in the left costophrenic angle. There was slight shift of the mediastinum to the right and marked subcutaneous emphysema. There was a splintered fracture of the eighth left rib just behind the posterior angle.

An occlusive dressing was applied to the thoracic wound. The left pleural cavity was needled and connected to an underwater drain. Oxygen was administered by B.L.B. mask, and one-sixth of a grain of morphine was given to alleviate anxiety. Tetanus antiserum, penicillin and streptomycin were also given.

On this regime the patient slowly improved. X-ray examination of her chest on November 27 showed an increase in fluid at the base of the left lung, and 10 ounces of blood were aspirated. The patient ran a temperature of up to 101° F., but this settled during the next 19 days. The only other complication was an attack of phlebothrombosis in the left calf, which resolved on anticoagulant therapy.

Ten days after injury the pneumothorax had cleared, but the lower half of the lung field was still hazy. When followed up in January, 1958, the patient was fit, but there was still reduced movement and air entry at the base of the left lung due to a small pleural effusion. In February the patient had remained well and the effusion had almost resolved.

This was the only case of open pneumothorax in the series, and the patient was initially seriously ill, probably as a result of mediastinal flap. Once the pneumothorax was closed her condition improved. The hæmothorax delayed recovery, but was adequately treated by aspiration.

CASE V.—A man, aged 64 years, was admitted to hospital on November 24, 1957, having been knocked from his bicycle by a car.

On examination his temperature was 98·4° F., his pulse rate 80 per minute and his respiration rate 20 per minute. His blood pressure was 130/90 mm. of mercury. There was an obvious right pneumothorax, together with multiple fractured ribs on the right side.

X-ray examination revealed a 50% right pneumothorax with anterior stove-in injuries of the right second and third ribs, together with double fractures of the fifth, sixth, seventh, eighth and ninth right ribs. There was no mediastinal shift, but a small amount of fluid was present in the right pleural cavity, together with mild subcutaneous emphysema. In addition, there was a fracture of the right tibia and fibula six inches below the knee.

The pneumothorax was connected to an underwater drain. The patient was then anæsthetized and the tibiofibular fracture reduced. Penicillin and streptomycin were administered. The patient made a good immediate recovery, but suddenly became shocked and dyspnœic 48 hours after injury. The wall of the right side of the chest was found to be obviously unstable and was moving paradoxically.

X-ray examination showed a 75% right pneumothorax with slight mediastinal shift to the left.

Hooks were inserted under the third and fourth right ribs anteriorly, and attached to two pounds' traction to stabilize the chest. The right lung was drained by a catheter attached to suction. These procedures improved the patient's condition, and the pneumothorax decreased to 25%. On December 3 a hæmoptysis occurred, and on December 6 he became suddenly shocked and died 24 hours later.

Autopsy revealed a large myocardial infarction as the cause of death. The presence of double fractures of the fifth, sixth, seventh and eighth ribs was confirmed. The right lung showed marked collapse of the lower lobe, but there was no obvious area of lung damage.

The effects of flail chest developed late and were effectively controlled by traction. It is interesting to note that an anæsthetic was administered in the presence of a needled pneumothorax, without disturbing the patient.

Discussion.

A feature of this series is the association of a head injury and minor fractures of the thoracic cage with a pneumothorax in Cases I, II and III. In each case the upper ribs were fractured and in no instance were they displaced. The presence of a pneumothorax was discovered only by repeated X-ray examinations in Case I, and by systematic examination of the patients in Cases II and III, for symptoms attributable to a collapsed lung were minimal and tended to be overshadowed by the associated head injury.

For a pneumothorax to occur after a closed thoracic injury, there must be an air leak from the lung into the pleural cavity. This can occur in two ways. (i) At the time of fracture, the rib is sufficiently deformed to transgress the pleura and puncture the lung, returning to its normal position when the displacing forces cease. (ii) A blow on the chest, received when the glottis is closed, is sufficient to raise intrapulmonary pressure enough to rupture an alveolus or bleb on the pleural surface of the lung. If the theory of raised intrapulmonary pressure is correct, it must obviously be possible to develop a bilateral pneumothorax after injury to one side of the chest, for with the glottis closed the pressure increases will be equally distributed through both lungs. There is no such example in the series, but Mr. H. Gatenby has kindly allowed me to quote the case of a patient recently under his care. This case illustrates that bilateral pneumothorax can occur as a consequence of closed chest injury.

A boy, aged 15 years, was admitted to hospital on April 7, 1958, having been involved in a car accident. He had been knocked unconscious.

On examination his temperature was 98° F., his pulse rate 130 per minute and his respiration rate 40 per minute. His blood pressure was 150/70 mm. of mercury. The patient was conscious, but confused, and had bilateral orbital hæmatomata. There was respiratory distress and slight cyanosis requiring oxygen. He had also sustained a fracture of the left clavicle and of the right radius.

X-ray examination of the chest revealed a 50% pneumothorax on the left side with some subcutaneous emphysema. On the right there was a 10% pneumothorax, and the underlying lung showed the mottling of traumatic bronchopneumonia. There were also undisplaced fractures of the necks of the lower ribs on both sides. A further X-ray

examination of the chest 12 hours after his admission to hospital showed a shift of the mediastinum to the right and an increase in both pneumothoraces.

Both pneumothoraces were connected to underwater drains soon after the patient's admission to hospital. The left pneumothorax blew off under pressure, and this greatly relieved the patient. Both drains were connected to continuous suction, but despite this, tracheotomy was eventually necessary, in order to provide a more efficient airway and an easy path for aspiration of the bronchi. The patient made a slow but steady recovery, and was discharged from hospital 34 days after injury. At this time X-ray examination showed the left lung to be almost clear, but there was a shadow in the upper lobe of the right lung, thought to be due to a loculated hæmothorax.

A further interesting feature of this case was the beneficial (probably life-saving) effect of tracheotomy. This provided for more direct aeration of the partially collapsed lungs and allowed frequent bronchial toilet. Once again there was an associated head injury, although respiratory symptoms dominated the clinical picture.

The other case of closed pneumothorax had thoracic injuries sufficiently severe to direct attention to the chest. The presence of double fractures of the ribs resulted in an area of instability of the right hemithorax. This area was sucked in during inspiration and blown out during expiration, and the underlying collapsed lung had no chance to reexpand. Although there were multiple rib fractures, it is doubtful whether these caused the pneumothorax, for the X-ray pattern of the fractures suggested thoracic compression, and post-mortem examination revealed no evidence of laceration of the lung.

The only case of open pneumothorax presented the most urgent clinical picture, in which dyspnœa and hypotension predominated. These symptoms were the consequence of mediastinal flap, which is always liable to occur in an open pneumothorax unless the mediastinum is rigid.

Symptoms and Signs.

It is obviously futile to rely on symptoms of respiratory distress to suggest the presence of a pneumothorax. Only in Case IV was the respiratory rate raised when the patient was admitted to hospital. However, in all except Case I a pneumothorax was clinically evident on careful examination of the chest. In Cases II and IV the presence of subcutaneous emphysema lent weight to the diagnosis.

X-ray examination of the chest provided the most accurate information, not only about the presence of pneumothorax but also about its extent, the presence of pleural effusion and the degree of mediastinal shift.

Treatment.

An open pneumothorax must be closed at the earliest opportunity to avoid the dangers of mediastinal flap. In an emergency this is best performed by the application of a "Vaseline" pack to the thoracic wound. Once the patient is in hospital the wound can be formally excised and sutured. On rare occasions a limited thoracotomy may be indicated for the removal of blood clot or a foreign body. It is advisable to drain the pleural cavity to a water-sealed system after such a procedure. Drainage is assured and pulmonary expansion assisted.

The closed pneumothorax may need no treatment whatsoever, especially if it is incomplete. Provided the pulmonary leak does not persist, the air in the pleural cavity will steadily absorb. It is important to check the rate of absorption by regular X-ray examinations of the chest, for the longer the lung remains collapsed, the more likely is permanent pulmonary damage such as fibrosis and bronchiectasis to occur. Persisting pulmonary collapse must be treated by pleural needling and bronchoscopic aspiration, for it may be due to a continuing pulmonary leak or a bronchial mucous plug.

The pain of fractured ribs is better relieved by the injection of a local anæsthetic into the fracture site than by cumbersome strapping, which tends to restrict movement of the uninjured side of the chest. Morphine or pethidine can be used to control severe pain. Oxygen should be given if indicated by the presence of cyanosis.

Underwater drainage following needle puncture was used in this series to encourage more rapid absorption of the pneumothorax. The results indicate that it is of value in this respect and may contribute to the prevention of late pulmonary complications. The disadvantages of needle puncture — hæmorrhage and infection — can be avoided by careful attention to technique. Twenty-four hours of underwater drainage suffices to eliminate the average pneumothorax. Stubborn cases can be encouraged to resolve by the application of suction (15 cm. of water) to the drainage bottle.

Whilst needling is not essential in the average case, it is urgent and sometimes life-saving in a tension pneumothorax (Case III) where air will blow off under pressure as soon as the pleural cavity is tapped, with immediate relief of dyspnœa.

Pleural effusions usually develop late and only need aspiration if they are large enough to cause symptoms. Hæmothorax may accompany the original injury and should be aspirated dry. Empyema may develop, especially in an open pneumothorax, and should be treated by accepted principles.

Concomitant injuries must be treated in order of priority, and it should be noted that needling of the pneumothorax is no contraindication to careful general anæsthesia.

No patient in this series has developed permanent lung damage, but no doubt if a sufficiently large number of cases were studied, the need for thoracotomy and decortication would be found to arise in a small proportion.

Complications.

The complications that developed are as follows: tension pneumothorax, Case III; pleural effusion (small), Cases I and III; hæmothorax, Case IV; flail chest, Case V; hæmoptysis, Case V; shock (early), Case IV; shock (late), Case V (coronary occlusion); slow resolution, Cases I and III.

Dangers.

The dangers of traumatic pneumothorax can occur early or late. The early causes of death are shock and anoxia. These result from bleeding into the pleural cavity, from tension pneumothorax and from mediastinal flap. The late danger is that of restricted pulmonary function due to fibrosis and bronchiectasis. This can be avoided by correct early management directed at reexpansion of the lung as soon as possible.

Conclusions and Summary.

Traumatic pneumothorax appears to be a frequent accompaniment of multiple injuries, which may initially overshadow it.

There is often little thoracic bony injury to account for the development of pneumothorax, which must be due to a sudden increase of intrapulmonary pressure.

Needling of the pleural cavity, combined with underwater drainage, encourages reexpansion of the lung, thus minimizing late complications.

Provided that the possibility of traumatic pneumothorax is borne in mind in any case of multiple injury, it will rarely remain undiagnosed.

OBSERVATIONS ON THE THIRD STAGE OF LABOUR WITH REFERENCE TO THE MODE OF PLACENTAL EXPULSION.

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EVER since Matthews Duncan (1871) described the type of placental separation known by his name, the belief has been held that the blood loss and morbidity with this type of separation are greater than with the mechanism described by Schultze (1867). Published work on this subject has so far tended to support this belief.

Pastore (1936), in a survey of 574 cases, reported an average loss of 231 ml. with the Schultze mechanism and

TABLE I.
Matthews Duncan Mechanism (176 Cases).

Method of Delivery of Placenta.	Number of Cases.	Average Blood Loss. (Oz.)	Duration of Third Stage. (Min.)	Post-Partum Hæmorrhage. (20 Oz. or More.)	Loss "Nil".	Placenta and Membranes Complete.	Membranes "Ragged".	Membranes Incomplete.
Brandt-Andrews	81	4·66	4·16	2	2	58 (71·6%)	22 (27·13%)	1
Fundal pressure	91	5·9	6·52	3	1	61 (67·03%)	29 (31·86%)	1
Spontaneous	4	2·75	4·25	0	0	3	1	0
Total	176	5·66	5·67	5	3	122 (69·31%)	52 (29·54%)	2

269 ml. with the Matthews Duncan type; the respective incidences of post-partum hæmorrhage were 4·67% and 5·51%.

Abramson and Berman (1938), in a study of 1658 cases, recorded an average loss of 203 ml. with the Schultze type of placental separation and 270 ml. with the Matthews Duncan mechanism.

R. C. Brown *et alii* (1942), in a study of 246 cases, stated that of 101 patients who expelled the placenta Matthews Duncan fashion, 78 lost blood in the third stage of labour "of noteworthy amount". Of the 145 who expelled the placenta Schultze fashion, only 17 had "excessive blood losses". Nineteen post-partum hæmorrhages of 20 oz. or more were recorded, and all these occurred in cases in which the placenta had been expelled by the Matthews Duncan mechanism.

Burton Brown (1949), in her radiological study of separation of the placenta in 13 cases, gave the average loss in the third stage as 6 oz. with a Schultze separation of the placenta and 12 oz. with the Matthews Duncan mechanism.

The purpose of this article is to present a statistical survey with observations on the third stage of labour. A study was made of all deliveries at the Gables Maternity Hospital and Thorpe Hall Obstetric Annexe, Peterborough, over a period of ten months; only normal deliveries were selected for this report—a total of 700 cases. Forceps deliveries, breech deliveries and those in which manual removal of the placenta was performed were discounted, as also were all those cases in which the third stage blood loss had been estimated only and not accurately measured. The observations made were on the method of delivery of the placenta, the manner of its expulsion (whether by the Matthews Duncan or Schultze mechanism), the blood loss, and the duration of the third stage of labour. Observations were also made on the condition of the placenta and membranes (whether complete, ragged or incomplete), and these findings were correlated with the normality or otherwise of the puerperum.

In every case ergometrine (0·5 mgm. by intramuscular injection) together with hyalase (1500 units) was given at the delivery of the head (Kimbell, 1954).

The object of this survey is to compare and contrast the Matthews Duncan and Schultze types of expulsion of the placenta with reference to (*a*) the blood loss, (*b*) the duration of the third stage, (*c*) the condition of the placenta and membranes, and (*d*) the post-partum recovery of the patient.

The results of the survey are presented in Tables I and II.

In the two cases in Table I in which retention of membranes occurred, one patient had a post-partum loss of 24 oz. and the other had a loss of 6 oz. Both were pyrexial until the fourth day of the puerperium, when both passed large pieces of membrane. Neither patient required blood transfusion. The puerperium of each of the other four patients who had post-partum hæmorrhage was uneventful; none of these patients required blood transfusion.

In the one case in Table II in which retention of membranes occurred, the patient had a post-partum loss of 20 oz., but was not pyrexial in the puerperium and passed the membrane on the fourth day. One patient, who had a post-partum loss of 24 oz., required a transfusion of three pints of blood and was pyrexial for 36 hours after delivery. Of the other patients who had post-partum hæmorrhage, two who had losses of 22 and 21 oz. respectively required blood transfusions of one pint, and one of these was pyrexial in the puerperium; the cause was found, by exclusion, to be a cracked right nipple with mild infection, which responded to penicillin. All the other patients with post-partum hæmorrhage had normal, uneventful puerperia.

The blood losses in the third stage, the state of the placenta and the duration of the third stage are compared in Table III.

Discussion.

Study of the figures given in the present survey will reveal that the difference in blood loss in the third stage of labour with the two types of expulsion is of the order of 1 oz.; therefore, the loss with the Matthews Duncan mechanism is not markedly greater than with the Schultze mechanism. Also, the third stage is not appreciably longer, the Matthews Duncan mechanism requiring only 0·68 minute more than the Schultze type of expulsion.

Further study of the figures given does, however, reveal that there is a greater likelihood of torn membranes with

TABLE II.
Schultze Mechanism (524 Cases).

Method of Delivery of Placenta.	Number of Cases.	Average Blood Loss. (Oz.)	Duration of Third Stage. (Min.)	Post-Partum Hæmorrhage. (20 Oz. or More.)	Loss "Nil".	Placenta and Membranes Complete.	Membranes "Ragged".	Membranes Incomplete.
Brandt-Andrews	285	4·57	4·59	7	8	261 (91·58%)	24 (8·42%)	0
Fundal pressure	230	4·21	4·71	4	3	206 (89·56%)	23 (10·0%)	1
Spontaneous	9	8·66	8·4	1	0	6	3	0
Total	524	4·86	4·99	12	11	473 (90·26%)	50 (9·54%)	1

ILLUSTRATIONS TO THE ARTICLE BY MALCOLM COPPLESON.

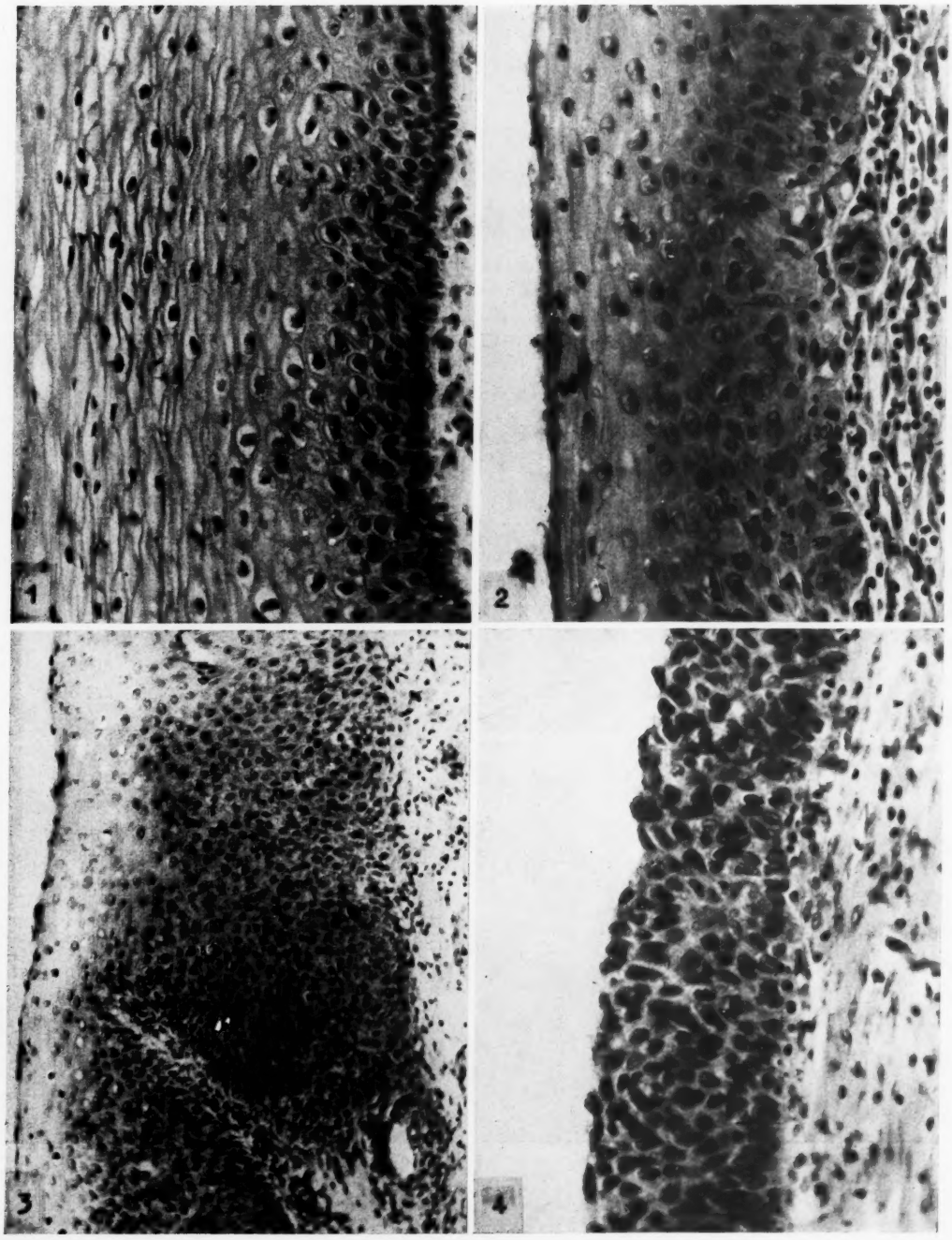

FIGURE I.—Normal squamous epithelium of the cervix. FIGURE II.—Simple atypical hyperplasia—slight increase in activity of the basal cells. FIGURE III.—Marked atypical hyperplasia—greater activity of the basal cells. FIGURE IV.—Carcinoma-in-situ—full-thickness involvement of the epithelium with atypical cells.

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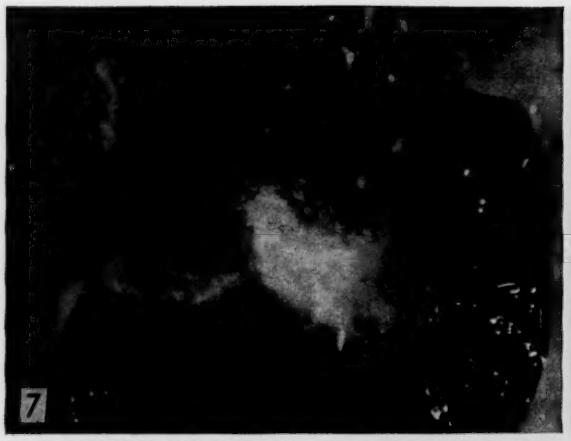

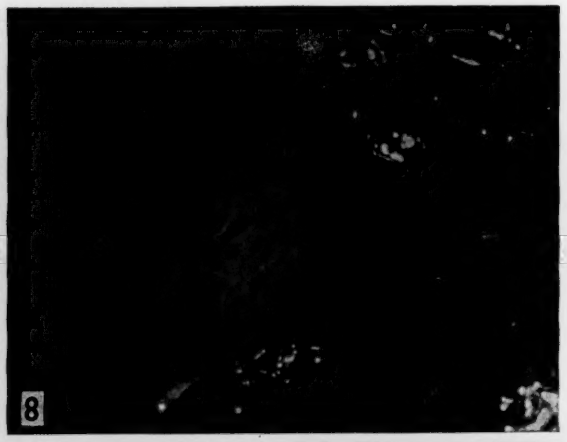

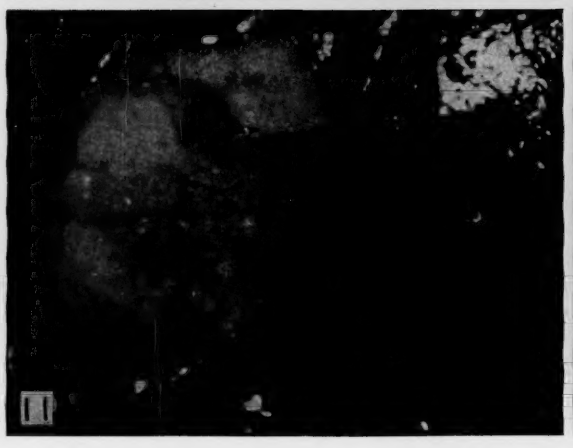

FIGURE VII.—Ectopic columnar epithelium around cervical os. Typical grape-like structure. Some mucus and contact bleeding can also be seen. FIGURE VIII.—Healing erosion (transformation zone), well developed, with squamous epithelium almost back to external os. Several gland openings and one Nabothian follicle can be seen. FIGURE IX.—Atrophic cervicitis. Thin epithelium with subepithelial hæmorrhages. Two small polypi can be seen near the external os. FIGURE X.—True erosion. An area devoid of epithelium on the anterior lip. Here the normal squamous epithelium at its edge indicates that the area is almost certainly benign. Several Nabothian follicles (out of focus and so simulating leucoplakic areas) can be seen. FIGURE XI—Leucoplakia. Large area of leucoplakia on anterior lip of cervix. Histological examination showed carcinoma-in-situ. FIGURE XII.—Mosaic structure, seen here after the application of Schiller's solution. Histological examination showed this area to be an early invasive carcinoma. (In Figures VII to XII the scattered white patches are due to light reflection.)

ILLUSTRATIONS TO THE ARTICLE BY N. McK. BENNETT.

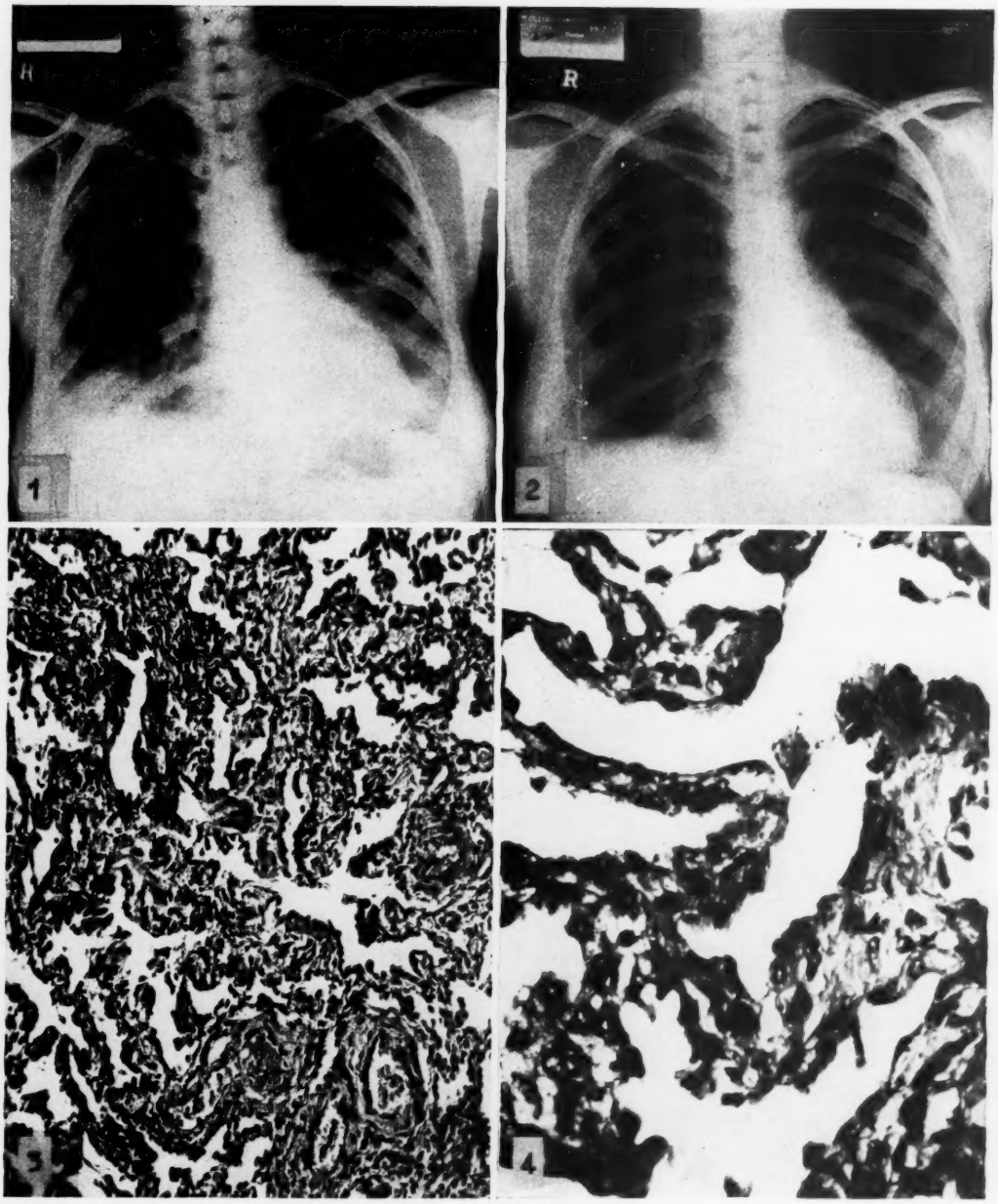

FIGURE I.—Skiagram of the patient's chest before lung biopsy and steroid therapy, demonstrating diffuse opacities at both bases. FIGURE II.—Skiagram of the chest after five months' steroid therapy; the lung fields have cleared considerably. FIGURE III.—Microscopic appearance of the lung biopsy specimen in the case described, showing thickened alveolar walls and thickened pulmonary arteries (×120). FIGURE IV.—High-power view of the lung biopsy specimen, showing that the alveolar walls are thickened by young fibrous tissue (×240).

ILLUSTRATIONS TO THE ARTICLE BY GODFREY HARRIS.

FIGURE I.
Air-contrast X-ray film showing polypi throughout the colon (July 4, 1958).

FIGURE II.
Notice the "short, narrow, low colon" (thought by some to be a stage of the disease), May 8, 1958, after passage of barium enema.

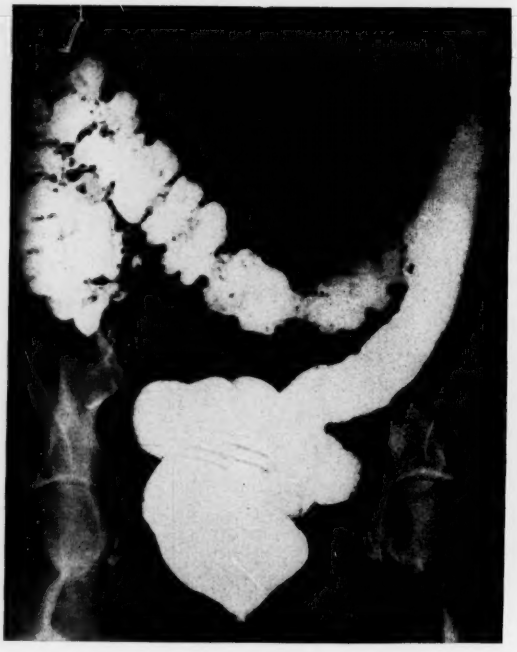

FIGURE III.
The colon appears to be longer and wider, and is higher under load. (In all these pictures, the degeneration of the colonic mucosa in the characteristic region is well demonstrated.) May 8, 1958; before passage of barium enema.

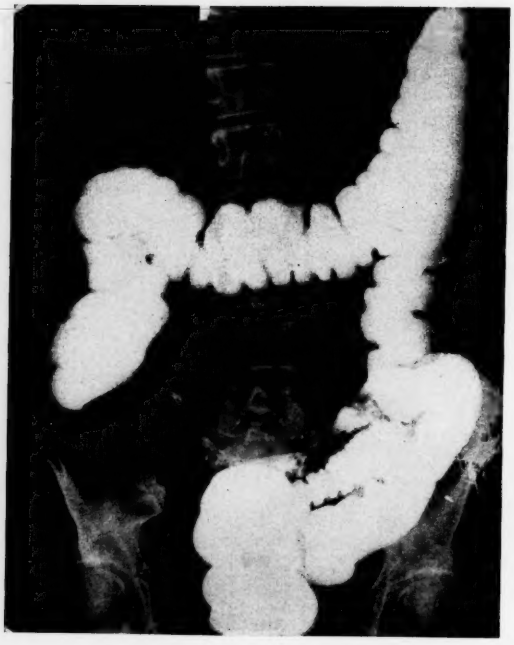

FIGURE IV.
A striking example, in another patient, a woman, aged 34 years, of mechanical involvement of the caecum in regional ileitis with symptomatic mimickry of ulcerative colitis. (The string lesion of Crohn's disease is excellently shown.)

a Matthews Duncan than with a Schultze placental expulsion.

One more fact emerges from the figures given: it will be noted that in 14 cases the loss was recorded as "nil". This fact is worthy of mention, in that it shows that the placenta does sometimes separate without any accompanying blood loss.

Frankl (1921) held that the formation of a retroplacental hæmatoma was a necessary factor in the mechanism of placental separation; subsequent writers tend to support this view (e.g., Brown *et alii*, 1942) with one or two exceptions (e.g., Titus and Andrews, 1924). The formation of a retroplacental hæmatoma cannot be a necessary factor in the mechanism of placental separation in cases in which there is no blood loss in the third stage of labour.

Finally, I should like to mention that the word "expulsion" as opposed to "separation" of the placenta has been used as far as possible in referring to my own observations, in the belief that the form which the placenta takes on extrusion at the vulva does not, of necessity, indicate its type of separation. For evidence in support of this statement reference may be made to the article by MacPherson and Wilson (1956), in which they recorded the results of their observations on the method of separation of the placenta.

TABLE III.

Mechanism of Expulsion.	Blood Loss. (Oz.)	Duration of Third Stage. (Min.)	"Ragged" Membranes.
Matthews Duncan ..	5·66	5·67	52 (29·54%)
Schultze	4·86	4·99	50 (9·78%)
Difference (by subtraction)	0·80	0·68	2 (19·81%)

Summary.

A study of the normal third stage of labour in 700 cases has been made. In every case, ergometrine (0·5 mgm. by intramuscular injection) with hyalase (1500 units) was given at the delivery of the head.

The blood loss occurring in the third stage with the Matthews Duncan type of expulsion of the placenta has been shown to be not appreciably greater than that with the Schultze mechanism.

There is very little difference in the duration of the third stage with the two types of expulsion.

However, it does seem that there is a greater likelihood of "ragged membranes" with a Matthews Duncan mechanism, but there is no increased liability to puerperal morbidity as judged by "pyrexia of uterine origin" or subsequent blood loss. In some of these cases there was no blood loss at all in the third stage of labour, and it is therefore suggested that the formation of a retroplacental hæmatoma is not a necessary factor in the mechanism of separation of the placenta.

Acknowledgements.

I wish to express my thanks to Mr. N. K. B. Kimbell, F.R.C.O.G., for his helpful advice and criticism, and to Miss J. M. Harrison for her help in the collection of data and preparation of this article for publication.

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CHRONIC MYELOID LEUKÆMIA: A STUDY OF 86 PATIENTS.[1]

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AND

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THE average length of survival of patients with chronic myeloid leukæmia is known with reasonable certainty, although the figures given by different authors show some variation (Table I). Nevertheless, it is difficult to predict

TABLE I.

The Duration of Survival from the First Symptoms.

Series.	Number of Cases.	Treatment.	Average Survival in Months from First Symptoms.
Minot, Buckman and Isaacs (1924).	78 52	Irradiation. No treatment.	42·0 36·0
Hoffman and Craver (1931) ..	82	Irradiation.	31·0
Leavell (1936)	87	Irradiation.	38·0
Lawrence *et alii* (1948) ..	129	P^{32}.	44·0
Wilkinson (1953)	69	HN^2.	29·0
Present series	86	Various, mainly irradiation.	35·0

the course of the disease in the individual patient, and to judge what the response to treatment will be. Some authorities doubt whether treatment of any kind prolongs life (Pascutti, 1942; Krebs and Bichel, 1947; Ledlie, 1953; Scott, 1957). In recent years the problem has been complicated further by variations in irradiation technique and by the upsurge of chemotherapy, so that some thought is required in selecting the best therapy for a particular patient. We have approached these problems by reviewing 86 patients with chronic myeloid leukæmia who were treated at Sydney Hospital from 1922 to 1958.

THE SELECTION OF PATIENTS.

Patients were accepted for this study only if they fulfilled certain clinical and hæmatological criteria. These standards were strict, and some genuine cases of the disease were probably excluded. This is inevitable in a retrospective investigation. Splenic enlargement was considered necessary in an untreated patient, and patients

[1] From the Department of Radiotherapy and the Hæmatology Clinic, Sydney Hospital.

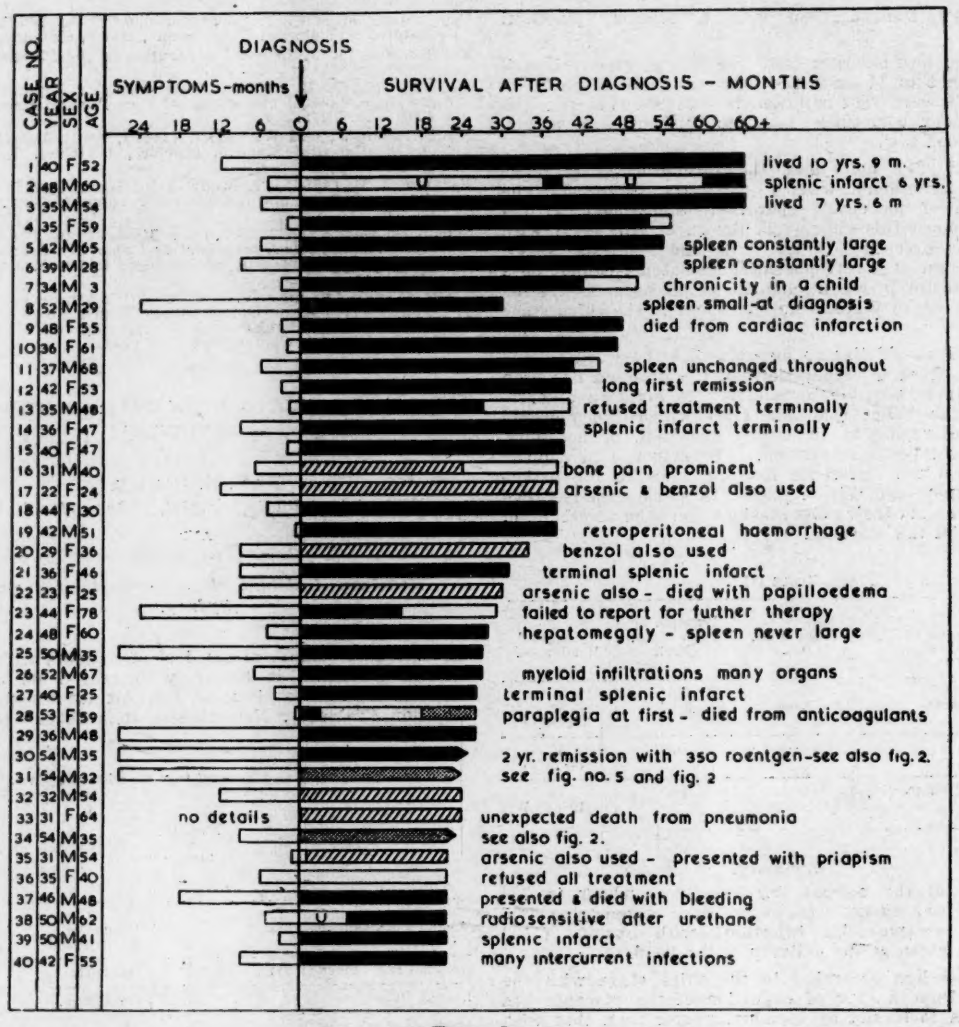

CASE NO.
YEAR
SEX
AGE
DIAGNOSIS
SYMPTOMS-months
SURVIVAL AFTER DIAGNOSIS - MONTHS
24 18 12 6 0 6 12 18 24 30 36 42 48 54 60 60+
1 40 F 52 lived 10 yrs. 9 m.
2 48 M 60 splenic infarct 6 yrs.
3 35 M 54 lived 7 yrs. 6 m
4 35 F 59
5 42 M 65 spleen constantly large
6 39 M 28 spleen constantly large
7 34 M 3 chronicity in a child
8 52 M 29 spleen small-at diagnosis
9 48 F 55 died from cardiac infarction
10 36 F 61
11 37 M 68 spleen unchanged throughout
12 42 F 53 long first remission
13 35 M 48 refused treatment terminally
14 36 F 47 splenic infarct terminally
15 40 F 47
16 31 M 40 bone pain prominent
17 22 F 24 arsenic & benzol also used
18 44 F 30
19 42 M 51 retroperitoneal haemorrhage
20 29 F 36 benzol also used
21 36 F 46 terminal splenic infarct
22 23 F 25 arsenic also - died with papilloedema
23 44 F 78 failed to report for further therapy
24 48 F 60 hepatomegaly - spleen never large
25 50 M 35
26 52 M 67 myeloid infiltrations many organs
27 40 F 25 terminal splenic infarct
28 53 F 59 paraplegia at first - died from anticoagulants
29 36 M 48
30 54 M 35 2 yr. remission with 350 roentgen-see also fig. 2.
31 54 M 32 see fig. no. 5 and fig. 2
32 32 M 54
33 31 F 64 no details unexpected death from pneumonia
34 54 M 35 see also fig. 2.
35 31 M 54 arsenic also used - presented with priapism
36 35 F 40 refused all treatment
37 46 M 48 presented & died with bleeding
38 50 M 62 radiosensitive after urethane
39 50 M 41 splenic infarct
40 42 F 55 many intercurrent infections

FIGURE Ia.

Table summarizing the course and treatment of 79 patients with chronic myeloid leukæmia. (For key see page 78.)

TABLE II.

The Frequency and Type of Presenting Manifestations.

Presenting Manifestations.	Number of Cases.
Symptoms of anæmia	67
Splenic tumour	39
Loss of weight	33
Splenic pain	30
Hæmorrhages[1]	28
Gastro-intestinal symptoms	18
Œdema of legs	16
Menstrual disturbances	7
Infections	7
Bone pain	6
Neurological symptoms including paraplegia	3
Priapism	2

[1] Hæmorrhages included subcutaneous bleeding (11 cases), epistaxis (5), retinal hæmorrhage (5), bleeding following tooth extraction (4), rectal bleeding (3).

TABLE III.

Types of Treatment Used.

Type of Treatment.	Number of Cases.	Remarks.
Low voltage X-ray therapy	16	Combined with arsenic and/or benzol in all but four cases.
Deep X-ray therapy alone	46	
Deep X-ray therapy *plus* other methods	8	
Arsenic	7	Combined with low-voltage X-ray therapy in all but one case.
Benzol	1	
Arsenic *plus* benzol	5	
Urethane alone	1	
Urethane *plus* other methods	4	
"Colcemid"	2	
"Myleran" alone	6	
"Myleran" *plus* other methods	4	
No treatment given	6	

with marked enlargement of the lymph nodes were discarded. Patients who survived for more than six years were also considered unacceptable when neither investigations nor autopsy had adequately excluded myelosclerosis.

The blood counts were required to conform to the usual textbook descriptions (Whitby and Britton, 1953; Wintrobe, 1956). When the leucocytes numbered less than 100,000 per cubic millimetre, the records were scrutinized with special care, and occasional patients were omitted

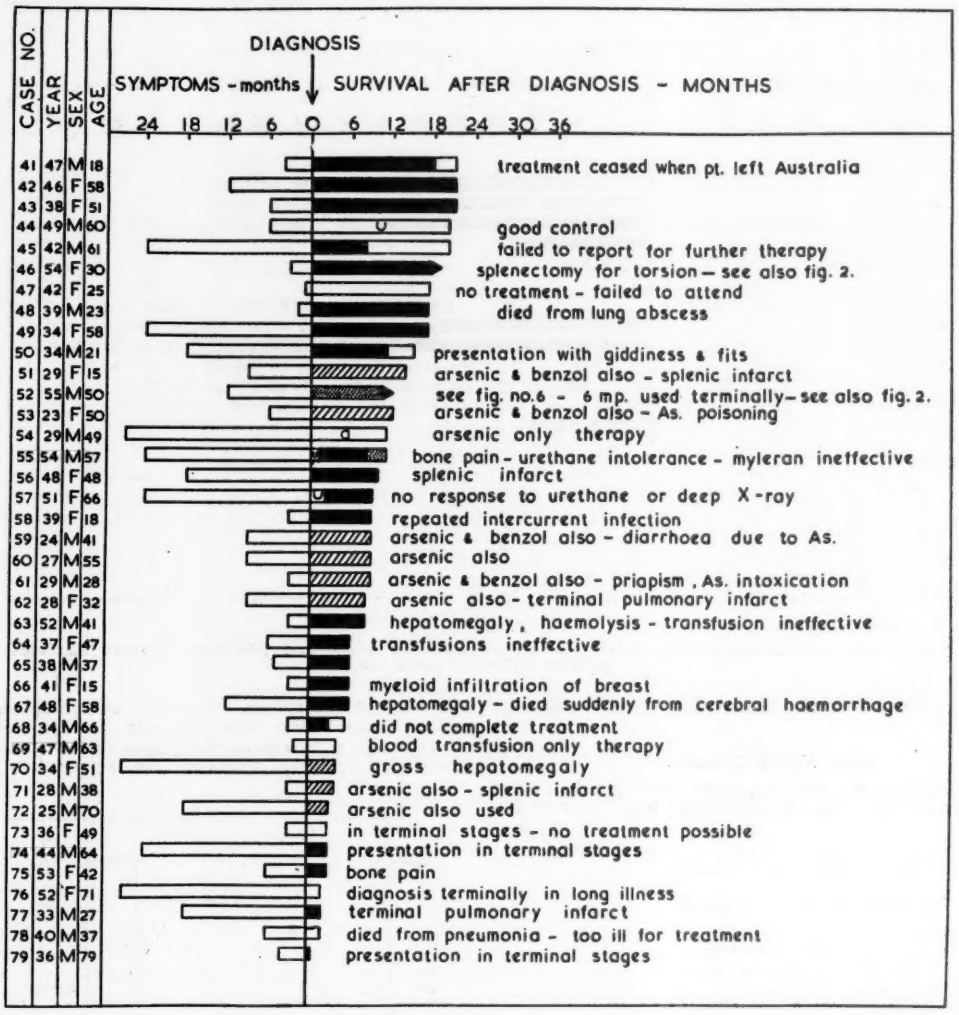

CASE NO.
YEAR
SEX
AGE
DIAGNOSIS
SYMPTOMS - months
SURVIVAL AFTER DIAGNOSIS - MONTHS
24 18 12 6 0 6 12 18 24 30 36
41 47 M 18 treatment ceased when pt. left Australia
42 46 F 58
43 38 F 51
44 49 M 60 good control
45 42 M 61 failed to report for further therapy
46 54 F 30 splenectomy for torsion — see also fig. 2.
47 42 F 25 no treatment - failed to attend
48 39 M 23 died from lung abscess
49 34 F 58
50 34 M 21 presentation with giddiness & fits
51 29 F 15 arsenic & benzol also - splenic infarct
52 55 M 50 see fig. no.6 - 6 mp. used terminally — see also fig. 2.
53 23 F 50 arsenic & benzol also - As. poisoning
54 29 M 49 arsenic only therapy
55 54 M 57 bone pain - urethane intolerance - myleran ineffective
56 48 F 48 splenic infarct
57 51 F 66 no response to urethane or deep X-ray
58 39 F 18 repeated intercurrent infection
59 24 M 41 arsenic & benzol also - diarrhoea due to As.
60 27 M 55 arsenic also
61 29 M 28 arsenic & benzol also - priapism , As. intoxication
62 28 F 32 arsenic also - terminal pulmonary infarct
63 52 M 41 hepatomegaly , haemolysis - transfusion ineffective
64 37 F 47 transfusions ineffective
65 38 M 37
66 41 F 15 myeloid infiltration of breast
67 48 F 58 hepatomegaly - died suddenly from cerebral haemorrhage
68 34 M 66 did not complete treatment
69 47 M 63 blood transfusion only therapy
70 34 F 51 gross hepatomegaly
71 28 M 38 arsenic also - splenic infarct
72 25 M 70 arsenic also used
73 36 F 49 in terminal stages - no treatment possible
74 44 M 64 presentation in terminal stages
75 53 F 42 bone pain
76 52 F 71 diagnosis terminally in long illness
77 33 M 27 terminal pulmonary infarct
78 40 M 37 died from pneumonia - too ill for treatment
79 36 M 79 presentation in terminal stages

FIGURE Ib.

Table summarizing the course and treatment of 79 patients with chronic myeloid leukæmia. (For key see page 78.)

from the series when it was found that conditions such as disseminated cancer, acute infection, generalized tuberculosis or myelosclerosis had not been adequately excluded. All cases in which the leucocytes on presentation numbered less than 10,000 per cubic millimetre were discarded, because, as most of these patients were treated when hæmatological investigation was incomplete by present standards, it was usually impossible to exclude conditions such as myelosclerosis and bone-marrow hypoplasia on the evidence available.

THE PRESENT SERIES.

General information about the series may be set out as follows:

Total number of patients accepted 86
Number still living 6
Number of autopsies performed 25
Sex incidence, male:female 44:42
Ratio of city to country patients 56:30

1922 N.S.W. census:

Metropolitan population ..... 923,650 (42·850%)
Rest of State ..... 1,321,872 (57·150%)

1954 N.S.W. census:

Metropolitan population ..... 1,865,860 (54·422%)
Rest of State ..... 1,562,628 (45·578%)

The slight predominance of male patients agrees with the findings of other authors (Wintrobe, 1956; Whitby and Britton, 1953). The age distribution is shown in Figure III, and again conforms with that found in other series (Gauld *et alii*, 1953). The presenting symptoms of our patients are shown in Table II. Further details concerning the duration of symptoms before diagnosis, the length of survival, the type of treatment and the present state of each patient are shown in Figures I and II.

Treatment.

Table III summarizes the methods of treatment used and the numbers of patients treated by each method.

Low Voltage X-Ray Therapy.

The X rays were generated at 100 kilovolts, the beam having a half-value layer of approximately 0·25 mm. of copper. The spleen was irradiated usually through an anterior field, occasionally through a lateral field varying

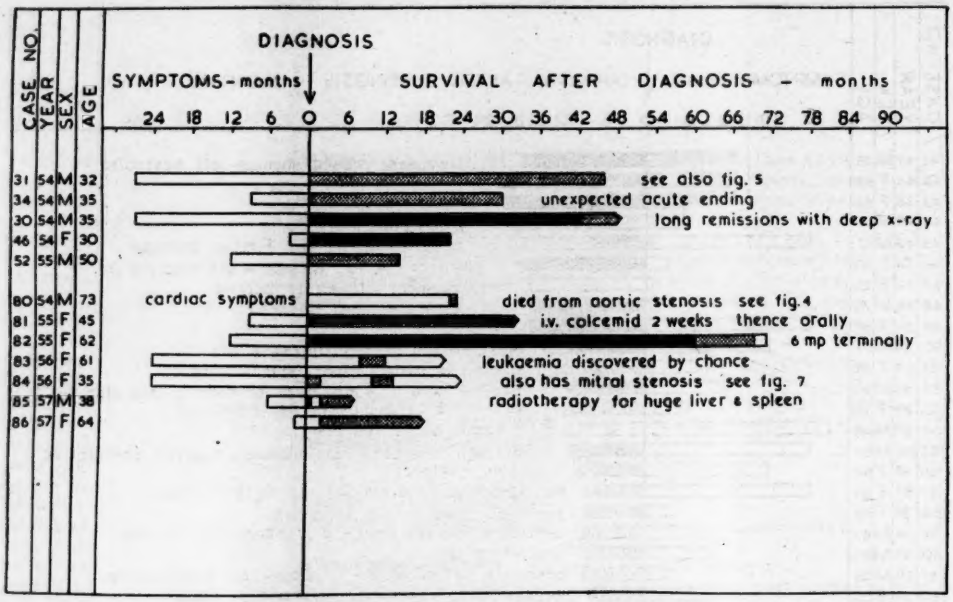

CASE NO.
YEAR
SEX
AGE
DIAGNOSIS
SYMPTOMS - months
SURVIVAL AFTER DIAGNOSIS - months
24 18 12 6 0 6 12 18 24 30 36 42 48 54 60 66 72 78 84 90
31 54 M 32
34 54 M 35
30 54 M 35
46 54 F 30
52 55 M 50
80 54 M 73
81 55 F 45
82 55 F 62
83 56 F 61
84 56 F 35
85 57 M 38
86 57 F 64
see also fig. 5
unexpected acute ending
long remissions with deep x-ray
cardiac symptoms
died from aortic stenosis see fig. 4
i.v. colcemid 2 weeks thence orally
6 mp terminally
leukaemia discovered by chance
also has mitral stenosis see fig. 7
radiotherapy for huge liver & spleen

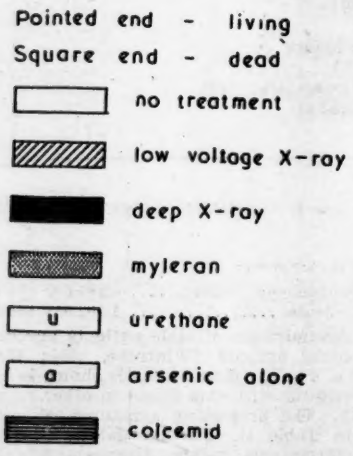
FIGURE II.

Table giving later details of five patients and summarizing the course and treatment of seven additional patients. (For key see below.)

in size from 10 to 15 cms. square. This method was used until 1935.

Deep X-Ray Therapy.

From 1935 onwards, an X-ray beam having a half-value layer of from 2 to 3 mm. of copper was used. At first the



Key to Figures I and II.

thorax was irradiated through anterior and posterior fields 15 cms. square. This technique was soon abandoned in favour of irradiation to the spine through long, narrow fields, usually 20 by 8 cms. in area. In 1940 splenic irradiation with field sizes as before was again adopted, and is still preferred.

The dose of X rays and the intervals between treatments varied enormously, depending on the patients' physical condition and the response. The daily skin dose was sometimes as low as 50*r* every two or three days when delivered to the spleen, the thorax or the spine, and was never higher than 200*r* per day to the spleen; but occasionally a maximum daily dose of 400*r* was given to the thorax or spine. The total dose required to produce a

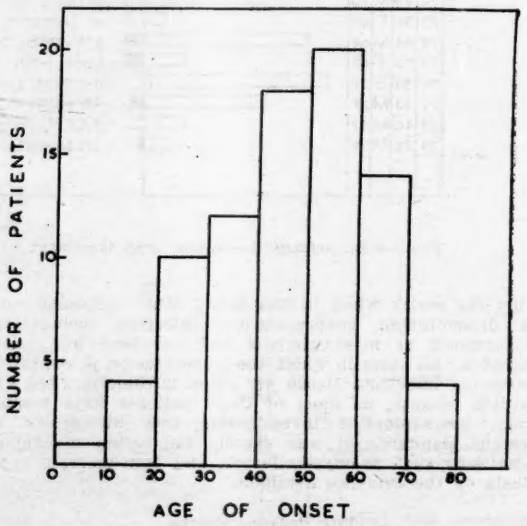


FIGURE III.

Graph showing the age incidence by decades in the present series.

remission varied just as widely. In Figures I and II, radiotherapy is shown for convenience in a continuous fashion; but treatment was always given intermittently.

Arsenic and Benzol.

These drugs were given orally to some of the earlier patients, and were usually combined with radiotherapy.

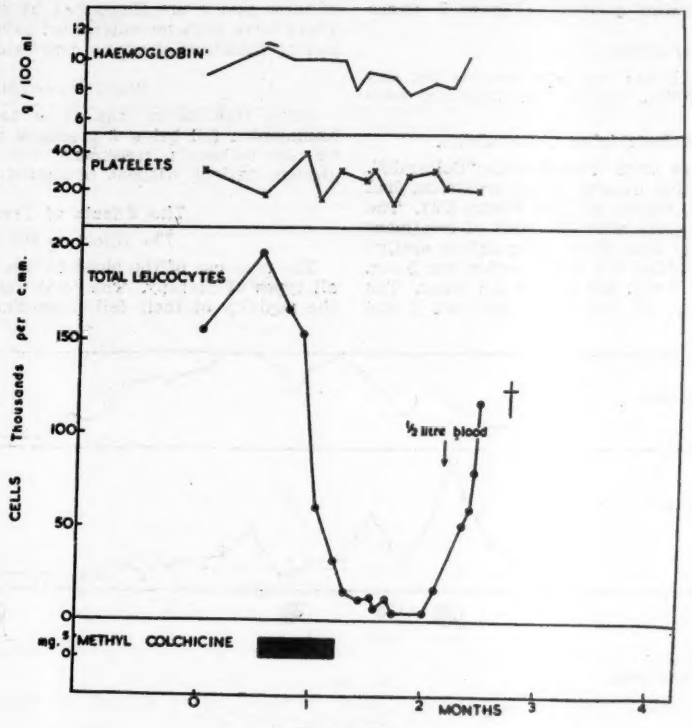


FIGURE IV.

Blood counts in Case 80, a patient treated with "Colcemid". Death was due to aortic stenosis.

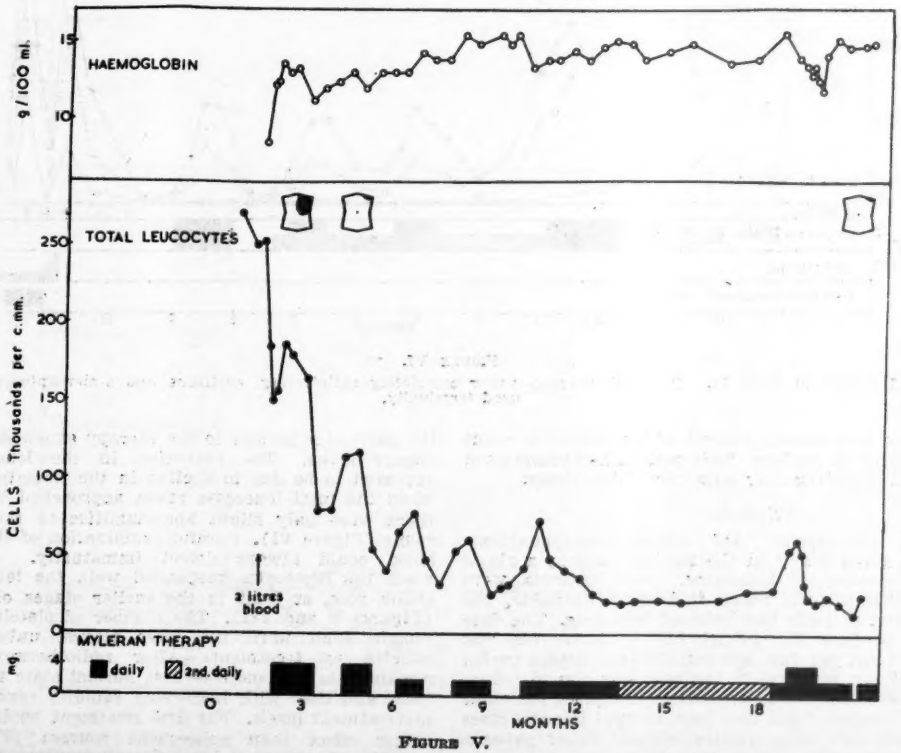


FIGURE V.

Blood counts in Case 31, a patient satisfactorily treated by continuous "Myleran" therapy.

Serious toxic reactions were common (Figure I, Cases 53, 59, 61).

Urethrane.

The usual dose of urethrane was one gramme per day given by mouth. Anorexia, nausea and vomiting were common.

"Colcemid" (Methylcolchicine, Demecolcin).

Two patients only have been treated with "Colcemid". One died from an unrelated disease before treatment had had a fair trial (Case 80, Figure II; also Figure IV). The other is still alive three years after the start of treatment (Case 81, Figure II). The dose of the drug (given orally) required to produce the initial fall of leucocytes was 5 mg. per day in one case and 6 mg. per day in the other. The maintenance dose in Case 81 has varied between 2 and 5 mg. per day, and smooth control of the leucocyte count has been difficult to achieve. This patient has complained of diarrhœa and falling hair with the higher doses.

"Myleran."

"Myleran" (busulphan, 1:4 dimethanesulphonyloxybutane) was given orally in the fasting state as a single dose each morning of treatment. Most patients were treated as out-patients. Since it became available, the therapy of most patients has included this drug. The dose required to produce the initial fall in leucocytes was usually 4 to 6 mg. per day, and maintenance dosage varied from 0·5 to 4 mg. per day. It has been our aim to reduce the number of leucocytes to approximately 10,000 per cubic millimetre. Treatment has then been stopped in some cases to be resumed only when relapse occurs. Other patients have been given continuous maintenance treatment. Some of these points are illustrated by Figures V, VI and VII. There have been no unpleasant symptoms in our patients, and no instances of undue depression of the bone marrow.

Blood Transfusion.

Blood transfusion was given to most patients whose hæmoglobin fell below 9 grammes per 100 ml. In general no anti-leukæmic treatment was given to a severely anæmic patient without preliminary transfusion.

The Effects of Treatment.

The Effect on the Blood.

The response of the blood to treatment was similar with all types of therapy. The total number of leucocytes fell, the rapidity of their fall depending on the sensitivity of the particular patient to the therapy employed and on the dosage given. The reduction in the leucocyte count appeared to be due to decline in the immature forms, as when the total leucocyte count approached normal levels there were only slight abnormalities in the differential count (Figure VI). Careful examination of the peripheral blood could always detect immaturity. Coincidently when the leucocytes responded well, the level of hæmoglobin rose, at least in the earlier stages of the disease (Figures V and VII). The number of platelets tended to remain high until the later stages, unless adversely affected by treatment. After radiotherapy the blood remained in this more or less normal state for a varying time, and then with increasing rapidity reverted towards pretreatment levels. The first treatment tended to cause a longer effect than subsequent courses (Figure VIII). Benzol and arsenic had a definite pancytopenic effect, with

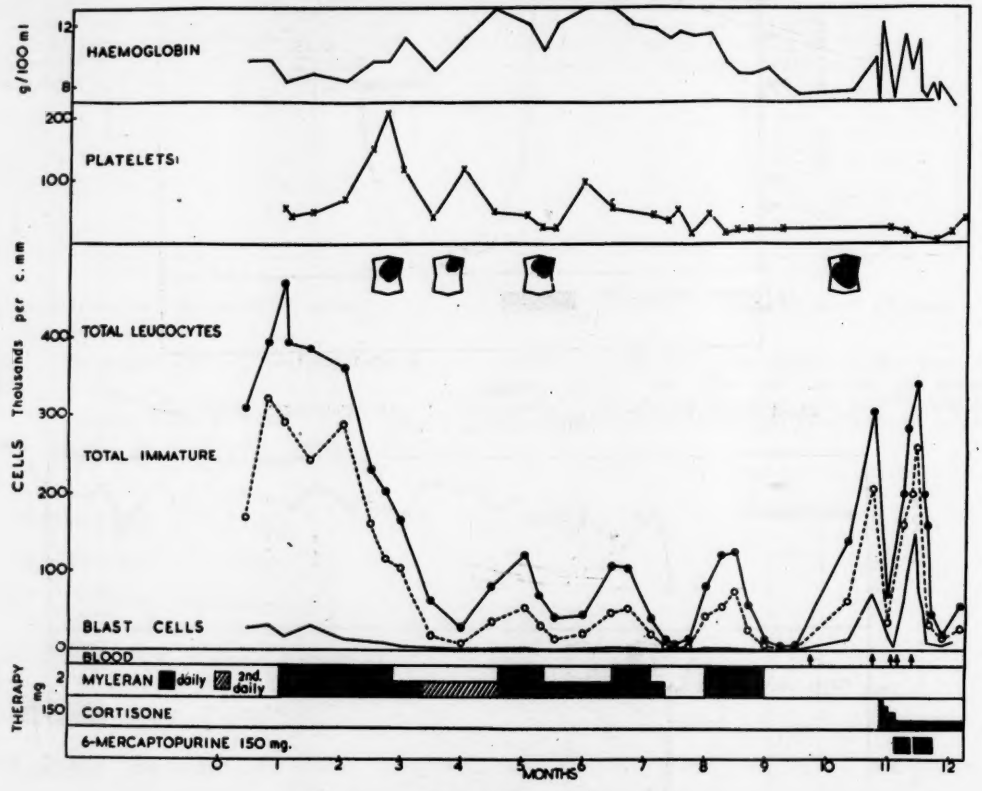


FIGURE VI.

Blood counts in Case 52, "Myleran" therapy never completely satisfactory, cortisone and 6-mercapto-purine used terminally.

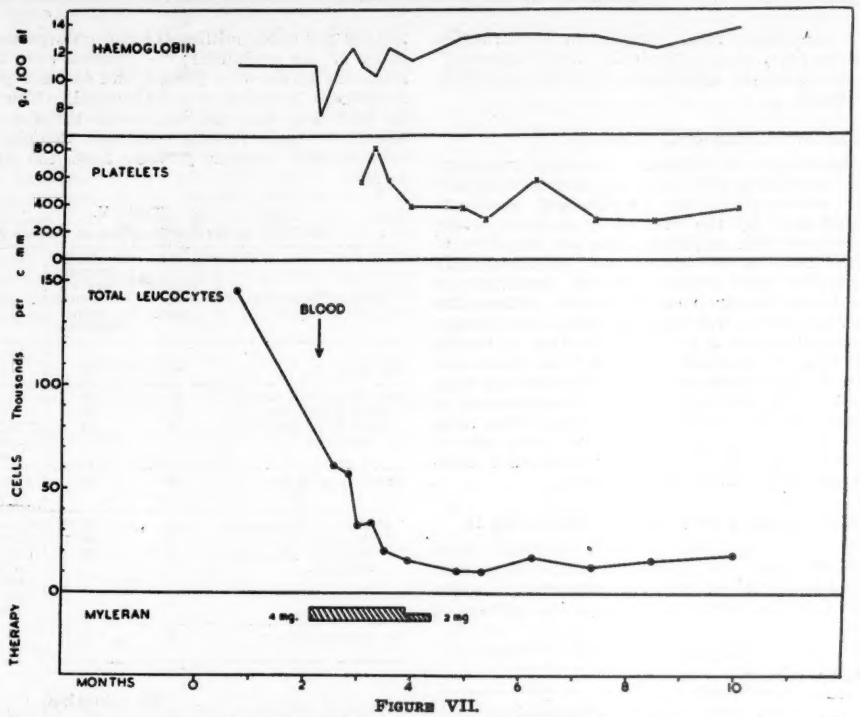


FIGURE VII.

Blood counts in Case 84, initial "Myleran" therapy followed by a long remission. No maintenance treatment given.

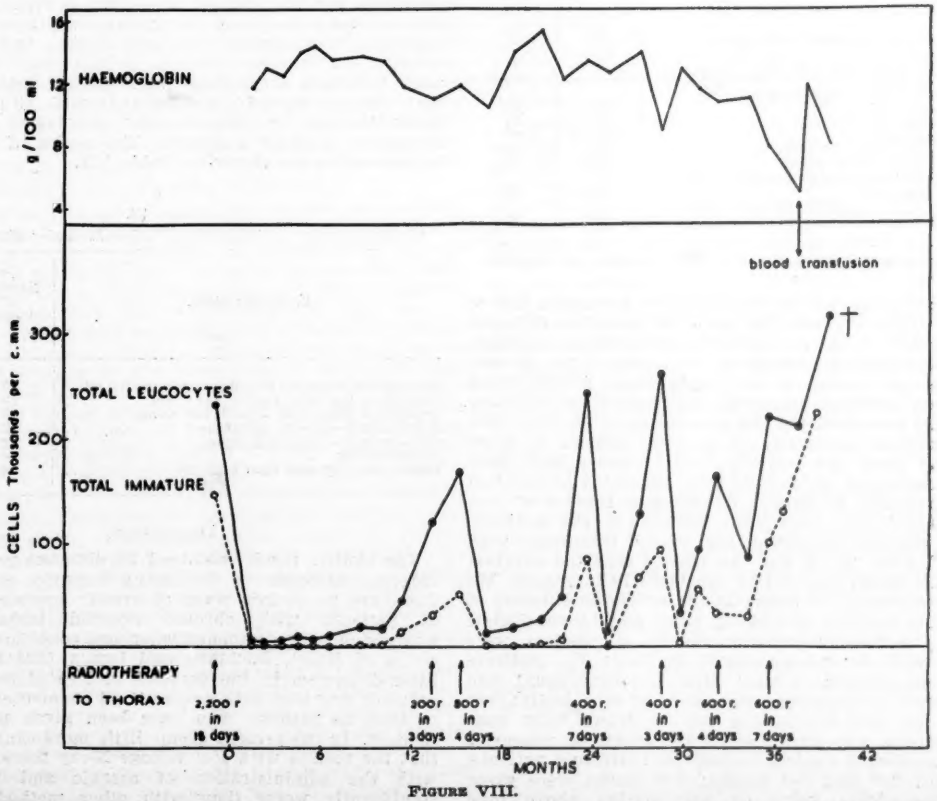


FIGURE VIII.

Blood counts in Case 12, a patient treated by radiotherapy showing shortening remissions and terminal resistance.

deleterious and sometimes fatal changes in erythrocytes and platelets at an early stage. "Myleran" and "Colcemid" depressed the granulocytes specifically without reduction of other components.

The Production of Remissions.

The remissions or periods of benefit following treatment were intimately concerned with both the blood count and other objective evidence of the disease, but could be accurately judged only by the over-all good done to the patient irrespective of the physical signs or the state of the blood. The lengths of remissions varied greatly amongst our patients, and accurate figures could not be obtained. A period of longer than six months without the need for further treatment was unusual with radiotherapy, and with the earlier, softer X rays the duration of benefit appeared much less. It was also apparent that irradiation of the thorax and spine produced shorter remissions than splenic irradiation. The remissions from chemotherapy in our patients could not be compared with those from deep X-ray therapy, because we have used the principle of initial treatment followed by immediate maintenance treatment for most patients having chemotherapy.

The Length of Survival and Factors Influencing It.

Our series has been analysed to discover what effect various factors, including the different types of treatment, had on the length of life of patients with this disease. Table IV shows that the survival time was not influenced

TABLE IV.

Periods of Survival of Different Groups.

Observation.	Number of Cases.	Months.
Average duration of symptoms before diagnosis ..	85[1]	10
Average length of life from first symptoms.. ..	85[1]	35
Average length of life from diagnosis:		
All patients	86	25
Male patients	44	24
Female patients	42	26
Patients aged under 40 years	27	22
Patients aged over 40 years	59	27
Patients with symptoms for less than six months before diagnosis	44	25
Patients with symptoms for more than six months before diagnosis	42	25

[1] In one case no details prior to the start of treatment were ascertainable.

by sex or age or by the duration of symptoms before diagnosis. Table V shows that patients treated by different methods mostly lived for much the same length of time, with the exception of those given low voltage X-ray therapy and those not treated at all. Both these groups fared badly. This probably indicates that modern radiotherapy has actually increased the life expectancy of patients with chronic myeloid leukæmia. It is more difficult to draw conclusions from the patients in this series who were given no treatment, as most of them presented in terminal stages. In Tables IV and V, all patients, those dead and the six still living, have been included in the analysis. Five of the six survivors are under treatment with "Myleran", from which one can deduce that the survival time of this group may yet be considerably increased. We have also attempted to ascertain the effects on survival of some of the common presenting signs and hæmatological findings. Thirty-four patients chosen at random were analysed, with the results shown in Table VI. Patients with severe anæmia, a very high leucocyte count and hepatomegaly at diagnosis appeared to fare badly; but obviously no firm conclusions can be drawn from such small numbers. Finally, to assess the effects on prognosis of combinations of clinical findings in individual patients, we allotted "+" and "–" marks; "+" marks were given for a hæmoglobin value on presentation above nine grammes per 100 ml., a total leucocyte count less than 250,000 per cubic millimetre and enlargement of the spleen short of the umbilicus; "–" marks were allotted if these arbitrary levels were passed, and also for presentation with significant bleeding or hepatomegaly. The most that could be said was that patients with three or more of these allegedly unfavourable findings usually survived for considerably shorter periods than the average for this series.

TABLE V.

The Effect on the Survival Time of Various Treatments.

Type of Treatment.	Number of Cases.	Average Survival in Months from Diagnosis.	Remarks.
All types	80	25	
Deep X-ray—*all patients*	54	29	
Deep X-ray alone ..	46	28	
Deep X-ray *plus* other methods.	8	33	"Myleran", 4 cases; urethane, 3 cases; both, 1 case.
Low-voltage X-ray ..	16	18	Arsenic and/or benzol used in 12 cases.
"Myleran"—all patients	10	27	Five patients still living.
"Myleran" alone ..	6	26	Three still living.
"Myleran" *plus* other methods.	4	29	Deep X-ray therapy, 3 cases; deep X-ray therapy and urethane, 1 case; 2 patients still living.
No treatment given ..	6	8	

Termination.

As the disease completes its course, resistance to treatment appears, and remissions are less complete, less sustained and with almost immediate rebound. The usual state at death is one of therapeutic resistance, malignant cachexia, a mounting leucocyte count, and increasing anæmia and thrombocytopenia. Intercurrent infection and acute leukæmia are common fatal complications. It seems that chronic myeloid leukæmia treated either by deep X-ray therapy or chemotherapy terminates with equal frequency in acute leukæmia. The modes of termination in this series are shown in Table VII.

TABLE VI.

The Effect on the Survival Time of Various Presenting Signs (34 Cases).

Presenting Signs.	Number of Cases.	Average Survival in Months from Diagnosis.
Hæmoglobin value less than 9 grammes per 100 ml. ..	*16*	*18*
Leucocytes less than 400,000 per c.mm.	19	22
Leucocytes more than 400,000 per c.mm.	15	13
Splenomegaly—ribs to umbilicus	12	27
Splenomegaly—below umbilicus	22	20
Hepatomegaly	14	16
Hæmorrhage (greater than bruising)	4	24

DISCUSSION.

The similar results obtained by different workers using different methods of treatment strongly suggests that there are no certain ways of greatly prolonging the life of patients with chronic myeloid leukæmia. This impression is strengthened when one considers that in the series of Minot, Buckman and Isaacs (1924), there was little difference in the survival of treated and untreated patients, and that both groups lived about the same length of time as patients who have been given more modern therapy. In the present group, little more can be said than that the results with low voltage X-ray therapy combined with the administration of arsenic and benzol seem significantly worse than with other methods, and that chemotherapy has given results comparable to those

achieved by radiotherapy. Soft X-ray therapy was inadequate by modern standards, and results may well have been made worse by the concomitant use of arsenic and benzol, as reports of toxicity were very common in the histories of these patients.

However, the effects of treatment are to be judged not only by length of life, but also by how well the patient feels during his remaining months, and whether he is able to keep on working. These are points about which it is impossible to produce actual figures; but there is no doubt in our minds that almost all patients were vastly improved in their general well-being and in their capacity to work. Indeed, most of our patients, at one time seriously incapacitated, have remained reasonably well and employed until close to their death. A New Guinea missionary (Case 31, Figures II and V), a man (Case 28) who at one time was paraplegic, and another (Case 81), still working three years after being admitted to hospital because of anæmia, amongst many other patients, illustrate this point well. Similarly, convenience, ease of administration and lack of unpleasant effects must be considered when one is judging whether methods of therapy have improved. By these standards modern chemotherapy, especially the use of "Myleran", is a step forward, as attendance at specialized centres is not necessary, or only occasionally necessary, there are no uncomfortable or dangerous side effects provided that the drug is used carefully, and there appears to us to be no more likelihood of acute leukæmia than with other treatment.

TABLE VII.
Termination and State at Death.

Termination.	Number of Cases.
Cachexia	34
Acute leukæmia	28
Intercurrent infection	23
Progressive anæmia	21
Hæmorrhage	17
Infarct:	
Splenic	9
Pulmonary	1
Renal failure	2
Ascites	2
Jaundice	1
Unrelated causes	3

The prognosis in chronic myeloid leukæmia is uncertain. Patients live on the average about two years from diagnosis, and this is all that one can positively say. In this present series the only patients who possibly fared worse than average were those who had severe anæmia, extreme leucocytosis or hepatomegaly at the time of diagnosis—signs which simply suggest advanced or swiftly progressive disease. However, these figures were drawn from too few cases to give more than an impression that prognosis was poor within this group. One is constantly surprised by a good response from patients least expected to do well, and disappointed by sudden fatal deterioration when the disease appeared well controlled. This occurred in Cases 8 and 34 (Figures I and II). The special hazards appear to be acute leukæmia and uncontrollable bleeding.

Our present impressions on the treatment of this disease can now be stated. Preliminary blood transfusion for the severely anæmic patient is considered important. We regard the use of "Myleran" as the treatment of choice for the reasons mentioned above. It is difficult to control the patient's condition smoothly with "Colcemid"; unpleasant side effects occur, and it has no advantages over "Myleran". We use radiotherapy only if there are focal pressure symptoms or vast hepato-splenomegaly, and then only for a short course. Pressure symptoms in our group have occurred in only two cases (28 and 82), and have been confined to the spinal cord. Deep X-ray therapy was used, because it was thought that the symptoms would probably be relieved most quickly in this way. We have used radiotherapy in the same way to achieve quick reduction of uncomfortable hepato-splenomegaly as a preliminary to treatment with "Myleran" (Case 85). We now try to reduce the total leucocyte count to approximately 10,000 per cubic millimetre, and to keep it at about this level—certainly less than 20,000 per cubic millimetre—by continuous minimal maintenance doses. There are good arguments for stopping treatment entirely when the original fall has been achieved, and recommencing it only when the number of leucocytes commences to rise steadily again. This was done in Case 84 (Figures II and VI). We have no evidence at present to state which method is better. Our experience is again slight; but when "Myleran" has ceased to be effective, our patients have died quickly, mostly because of acute leukæmia often complicated by hæmorrhage. Blood transfusion, steroid hormones and 6-mercaptopurine have been virtually ineffective in our hands in this situation. Deep X-ray therapy is not indicated when this chemical resistance develops, because the disease is moving fast and is often a frank acute leukæmia, and to our knowledge two patients (not included in this series) have been actively harmed by radiotherapy given under these conditions. In one rupture of the spleen occurred, and in the other there was a massive splenic infarct.

It is obvious that the current treatment of chronic myeloid leukæmia is unsatisfactory and prognostication difficult. Treatment makes the patient more comfortable, but improves his life expectancy very little. It appears to us that "Myleran" may eventually be found to improve this expectancy by a measurable amount; but it may also be that radiotherapy and the present methods of chemotherapy will eventually be discarded in favour of a more fundamental approach toward the problems of this disease.

SUMMARY.

A series of 86 patients with chronic myeloid leukæmia treated at Sydney Hospital between 1922 and 1958 has been reviewed.

The disease presented most commonly with symptoms of anæmia, noticeable abdominal swelling, pain or loss of weight. The sex incidence was approximately equal. All age groups were affected, but the peak incidence occurred between the ages of 40 and 60 years.

Patients survived on the average two years from the making of the diagnosis, and their span of life was little affected by sex, age or the duration of symptoms before diagnosis. The survival periods with most forms of treatment were approximately the same, although patients treated with low-voltage X-ray therapy combined with arsenic or benzol died sooner than other members of the series. Treatment with "Myleran" appeared to be at least as good as treatment by radiotherapy. There was also an indication that those patients with severe anæmia, marked leucocytosis or hepatomegaly at diagnosis had a poor prognosis, but the prognosis is very uncertain.

The disease terminated most commonly with malignant cachexia, acute leukæmia or intercurrent infection, and hæmorrhage remained a special hazard. Acute terminal leukæmia seemed to be part of the natural history of the disease, and not provoked by any specific form of treatment.

Patients can be treated most effectively with "Myleran", and deep X-ray therapy should be reserved for those with pressure symptoms or for the initial treatment of the grossly enlarged liver or spleen. When resistance to "Myleran" occurs, other chemicals are of limited use, and radiotherapy may be contraindicated.

ACKNOWLEDGEMENT.

We wish to thank the members of the Honorary Medical Staff of Sydney Hospital for their permission to cite some of the patients included in this report.

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Reports of Cases.

REPORT OF A CASE OF DIFFUSE INTERSTITIAL FIBROSIS OF THE LUNGS (HAMMAN-RICH SYNDROME) SUCCESSFULLY CONTROLLED BY PREDNISOLONE.

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Fairfield Hospital, Melbourne.

THE original descriptions of diffuse interstitial fibrosis of the lungs were made by Hamman and Rich in 1935 and 1944, and since that time more than 60 cases have been reported. The disease has been reviewed by Grant *et alii* in 1956 and by Rubin and Lubliner in 1957. The increasing number of reports suggests that this disease is not as rare as previously thought.

Clinically, the condition is manifested by progressive dyspnœa terminating in death by either respiratory or cardiac insufficiency. In most cases this dypsnœa is of relatively acute onset, but occasionally there is a long antecedent history. In addition to dyspnœa, cough, expectoration, chest pain, hæmoptysis and weight loss may occur.

These symptoms are commonly accompanied by cyanosis and clubbing of the fingers and toes. In the early stages, fever is not a feature and chest signs may be minimal, but in advanced stages of the disease with superimposed infection, signs of pneumonia and pleural effusion may occur. In these severe cases, failure of the right side of the heart may follow pulmonary hypertension. Most patients have died after a rapidly progressive illness, but some patients have survived for several years. There is no significant sex incidence, and most cases occur in the middle-aged and older age groups.

Skiagrams of the chest may show miliary, nodular or mottled opacities involving all or parts of both lungs. Frequently, these opacities occur in the basal segments, and in advanced cases areas of consolidation, pleural effusion and cardiac enlargement may be seen. Radiological changes in this disease are not specific, and a multitude of diseases can be simulated. In advanced stages, widespread "honeycombing" may be present, and rarely skiagrams of the chest may show no abnormalities. In one case the patient was initially regarded as a neurotic (Sloper and Williams, 1955).

The white cell count is generally not raised unless intercurrent infection is present. In long-standing cases there may be compensatory polycythæmia and electrocardiographic evidence of right ventricular strain.

The basic pathology was fully described in the original report by Hamman and Rich. Macroscopically, the lungs are firm, and the cut surface may show an interlacing fibrous network and often emphysema, bronchiectasis, bronchiolectasis or a honeycomb appearance (Forbes, 1958). Microscopically, various stages are apparent in the same lung. The early stages of the process are characterized by dilatation of alveolar capillaries, exudation of fluid and fibrin clotting. This is followed by the development of a hyaline membrane lining the alveoli. Cellular exudation consists of only a few polymorphs and mononuclears, whilst hæmorrhages into the alveoli are common. In places, epithelial cells lining the alveoli are swollen; in others necrosis is evident. The epithelium of the alveoli may be so hyperthrophied that the alveoli have a pseudo-glandular appearance. Changes may occur in the bronchiolar epithelium. Later, fibroblastic proliferation occurs. The alveolar walls and the hyaline membrane are replaced by fibroblasts, but there is little organization of the exudate in the alveoli. In later stages of the disease, the fibrous tissue becomes mature. In view of this fibrosis, the condition has been named "diffuse interstitial fibrosis of the lungs".

The physiological disturbance in the Hamman-Rich syndrome is ascribed to an "alveolar-capillary block". The diffusion of oxygen across the thickened alveolar-capillary membrane is impaired, but due to the greater diffusibility of carbon dioxide, diffusion of this gas is seldom impaired, except in the very late stages of the disease. The alveolar-capillary block syndrome consists of reduced lung volume, maintenance of a large maximum breathing capacity, hyperventilation at rest and during exercise, normal or nearly normal oxygen saturation at rest, but a marked reduction of arterial oxygen saturation after exercise, normal alveolar oxygen tension, a reduced oxygen diffusion capacity and pulmonary hypertension (Baldwin *et alii*, 1949; Austrian *et alii*, 1951).

Most of the early cases of the Hamman-Rich syndrome were diagnosed at autopsy. One of the earliest reports of ante-mortem diagnosis was made by Rubin *et alii* as late as 1952. Accumulating evidence suggests that the microscopic examination of tissue obtained by lung biopsy is necessary to confirm the diagnosis. Respiratory function tests may demonstrate an alveolar-capillary block, which is not specific to this syndrome.

The purpose of this communication is to describe a case of diffuse interstitial fibrosis of the lungs, the diagnosis of which was confirmed by open lung biopsy, and which has been satisfactorily controlled by adrenal steroids for nine and a half months.

Clinical Record.

On February 27, 1958, Mrs. A., aged 37 years, was admitted to Fairfield Hospital, Melbourne. She gave a history of approximately three weeks' shortness of breath, mainly on exertion, associated with a slight non-productive cough. On direct questioning she stated she had noted progressive shortness of breath for approximately two months. This shortness of breath had become so severe over the past three or four days that she was unable to stand or sit, and the only way she obtained any relief was to lie flat on her bed.

She had had no contact with air-borne dusts, beryllium or tuberculosis. There was no history of febrile episodes, purulent sputum, hæmoptysis or loss in weight. She had never had any serious illnesses or operations. Her family history was not unusual; her mother had died after a cerebral vascular accident and her father and a brother and sister were alive and well. She had two children, aged 15 years and 6 months respectively, who were both healthy.

The physical examination on admission to hospital was not very revealing. The temperature was 98·2° F., the pulse rate 88 per minute, blood pressure 130/80 mm. of mercury, and she weighed 136 lbs. There was marked clubbing of her fingers (the development of which she had noted over the last two months). Examination of

her chest revealed harsh breath sounds at both bases posteriorly, but no adventitiæ were heard. There was no significant lymphadenopathy. Examination of all other systems gave normal findings. Tests for albumin and sugar in her urine gave negative results. She had had an ichthyotic skin since birth and her brother had a similar skin.

Although some form of chronic lung disease was suspected, a course of penicillin given intramuscularly and tetracycline given orally was begun, with a diagnosis of probable bilateral bronchopneumonia. An X-ray examination of the chest on February 28 showed bilateral basal diffuse reticular opacities (Figure I). Mantoux skin tests with old tuberculin in strengths of both 1:1000 and 1:100 gave negative results. Her hæmoglobin value was 87% (12·9 grammes per 100 ml.) and the white cell count was 12,600 per c.mm. (80% neutrophil polymorphs). Nose and throat swabs produced no growth. The first 10 days of her stay in hospital were noticeable in that she remained afebrile, had only a slight non-productive cough and examination of her chest at no stage revealed adventitious sounds. At this stage the diagnosis of an infective lung condition was doubted. During this period she had a varying degree of shortness of breath. On some occasions she became short of breath when being sponged, but at other times she was able to walk several yards without undue distress.

On March 8 she had an incomplete abortion. Her last normal menstrual period was on December 30, 1957. On March 10, because of continued loss of blood she was transferred to the Royal Women's Hospital, Melbourne, for curettage. Gynæcologically, the curettage was uneventful, but considerable difficulty was met with in anæsthesia. She developed severe bronchospasm and cyanosis during induction of anæsthesia with "Pentothal", and during the first two post-operative days she remained a dusky colour, was quite short of breath on exertion, had a cough productive of white frothy sputum and several times needed positive pressure oxygen to keep her colour satisfactory.

On March 14 she was returned to Fairfield Hospital. On examination moderate cyanosis of her lips and fingers was noticeable. Examination of the chest showed it to be normal, she was afebrile, and apart from marked clubbing of her fingers, all other systems were normal. Now she became short of breath on mild exertion in bed, and this was accompanied by a deepening of her cyanosis. A skiagram of her chest was unchanged, attempts at culture of nose and throat swabs were unsuccessful, whilst a sputum culture revealed a mixed growth of *Streptococcus viridans*, pneumococci and diphtheroids, but no tubercle bacilli. She was then given erythromycin, 250 mg. every six hours. Next day very little improvement in her colour or exercise tolerance had occurred, and (in view of a possible cardiac lesion) she was given digitalis. Her electrocardiogram was normal. Over the following days no improvement occurred, and digitalis administration was discontinued.

Over the next two weeks her condition remained static. Shortness of breath and cyanosis occurred on undue exertion in bed, and her chest remained clinically clear and radiologically unchanged. She remained afebrile at all times, and had a slight cough producing only small amounts of white mucus. Her erythrocyte sedimentation rate was 2 mm. in one hour (Cutler tubes); microscopic examination of a centrifuged deposit of urine showed normal findings; L.E. cells were not detected in her peripheral blood; liver function tests gave normal results; absolute blood values were normal and the highest white cell count was 18,500 per c.mm. (with a shift to the left in neutrophil polymorphs). Skiagrams of her hands and feet were normal, and an X-ray examination with a barium swallow gave normal findings. Her blood urea content was 30 mg. per 100 ml. and urea clearance tests gave normal results. The serum protein content was 6·3 grammes per 100 ml. with normal fractions on electrophoresis. No malignant cells were seen in her sputum on successive examinations, and Wassermann and Kahn tests gave negative results. Studies for enteric virus infection also produced negative findings.

In view of the absence of clinical signs and the lack of information gained from special investigations, her diagnosis was considered to be some form of pulmonary fibrosis.

On March 31 she was transferred to the Alfred Hospital, Melbourne, where on April 4, an open thoracotomy was performed under general anæsthesia and a lung biopsy specimen was taken from the right lower lobe. Post-operatively she developed signs of a right lower lobe pneumonia, which responded to penicillin; otherwise her convalescence was uneventful. Microscopically, the lung showed marked and uniform thickening of alveolar walls by young fibrous tissue and also proliferation of alveolar epithelium. The small and medium-sized arteries showed medial and external thickening. The appearances were consistent with the diffuse interstitial fibrosis of lungs described by Hamman and Rich (Figures III and IV).

After a satisfactory post-operative convalescence she was readmitted to Fairfield Hospital on May 8. Apart from a recent well-healed right thoracotomy scar, her physical signs were unchanged. She could walk short distances, but at times easily became short of breath and cyanosed during mild activity in bed. On May 9 she was started on a course of prednisolone, 40 mg. daily in divided doses. Improvement in her exercise tolerance was noted within two weeks and she could then walk up two flights of stairs without undue distress or cyanosis. On May 30 she was discharged from hospital on 20 mg. of prednisolone daily in divided doses. On discharge, an X-ray examination of her chest still showed bilateral diffuse basal opacities, which were unchanged since her first admission to Fairfield Hospital.

Over the next two months she was observed closely as an out-patient at intervals of one to two weeks, and on July 4 she was readmitted to Fairfield Hospital for review. At this stage she had had 56 days' continuous treatment with prednisolone. During this period she had noted a remarkable improvement in her exercise tolerance. She was able to walk up to three miles on flat ground and do all her household work without severe shortness of breath. However, severe shortness of breath occurred when she attempted to run or walk up a fairly steep incline. She had had no cough or sputum since her discharge from hospital, but had noted an occasional right-sided pleuritic type pain on deep inspiration (this had occurred since thoracotomy). On examination she was a happy healthy-looking woman, with a temperature of 97° F., and a pulse rate of 88 and a respiratory rate of 20 per minute. Her weight was 133 lb. Clubbing of her fingers was much less marked, and no cyanosis was present (cyanosis had not been observed since her last admission to hospital). Examination of her chest and other systems showed no abnormalities. Apart from mild facial hirsutism and a rounded appearance of her face, there were no other side-effects of steroid therapy. A skiagram of her chest was unchanged since her original admission to hospital.

After a short stay in hospital she was discharged, and since July 5 she has been kept on a maintenance dose of 15 mg. of prednisolone daily. For the last six months up to the time of writing this paper she has been observed every two weeks. Further improvement in her exercise tolerance has occurred, so that now she has very little limitation of activity. The only physical abnormality detectable now is minimal finger clubbing. Continuous steroid therapy has now been administered for approximately nine and a half months. Serial X-ray examinations of the chest over the last few months have shown a steady decrease in the bilateral opacities, so that a skiagram taken on October 10 was reported as "lungs now clear, the right costo-phrenic angle is obliterated to a lesser degree" (Figure II). She is now enjoying full activity, and is approximately four months pregnant.

Limited respiratory function tests were performed in May, i.e., just after thoracotomy and after five months' treatment (Table I). The ventilatory studies before the commencement of cortisone therapy are consistent with a severe restrictive lesion. The compliance values show

a marked loss of pulmonary elasticity, but the value does not drop as in severe emphysema. This is in keeping with a fibrotic lesion. Alveolar-capillary block is not excluded by the data, but, unfortunately, the necessary blood gas analyses could not be carried out at the time, and no means were available for measuring the pulmonary diffusion coefficient which, in view of the diagnosis, would have been most valuable in the subsequent assessment of treatment.

After cortisone therapy, there was a tremendous improvement in ventilation, particularly in the maximum breathing capacity, the last result obtained being within normal limits for the machine used. The compliance studies, however, show a further drop and compliance decreased rapidly with an increase in respiratory rate. This suggested that emphysematous changes were occurring, but the suggestion is not borne out by the remainder of the study.

The pulmonary function tests in this patient were insufficient to demonstrate an alveolar-capillary block, which is associated with this syndrome. However, they do demonstrate the marked improvement in ventilation which has occurred after steroid therapy.

TABLE I.

Pulmonary Function Tests.

Pulmonary Function Tests.	Before Cortisone. (May, 1958.)	After Cortisone. (October, 1958.)
Inspiratory capacity ..	842 c.cm.	1804 c.cm.
Expiratory reserve volume	314 c.cm.	704 c.cm.
Vital capacity	1156 c.cm.	2508 c.cm.
Tidal volume	440 c.cm.	924 c.cm.
Minute volume	8·8 litres per minute.	17·6 litres per minute.
Maximum breathing capacity.	38·2 litres per minute.	96·8 litres per minute.
Spirogram	Normal.	Normal.
Compliance of lungs and thorax.	0·12 litre per cm. of water at 20 per minute. Average 0·11 litre per cm. of water over a range of 20 to 60 per minute.	0·06 litres per cm. of water dropping progressively to 0·023 at 70 per minute.
Oxygen saturation arterial blood, femoral sample, breathing air.	——	91%.

Discussion.

This case illustrates some of the characteristic features of diagnosis of the Hamman-Rich syndrome. When the patient was admitted to hospital a provisional diagnosis of bronchopneumonia was made, but after 48 hours' observation this was in doubt in spite of a suggestive X-ray film, because of the persistent absence of features characteristic of infection. Although her rapid clinical deterioration had previously suggested an acute pulmonary infection, she remained afebrile, her white cell count was low, there was little sputum, and her dyspnœa persisted in spite of treatment. Furthermore, the persistent absence of adventitious sounds in the chest was not in accord with this diagnosis. These unusual findings associated with marked dyspnœa, cyanosis and osteoarthropathy were noted by Hamman and Rich in their original report.

Bronchopneumonia has been the initial diagnosis in many reported cases; cardiac disease, which was also considered in this case, in others. Other not uncommon features demonstrated by this case are fluctuation in the severity of cyanosis and dyspnœa and an altered quality of the breath sounds over the involved parts of the lungs (Forbes, 1958).

The possible diagnoses were sarcoidosis, alveolar cell carcinoma, lymphatic spread of carcinoma, tuberculosis, inhalational lung disease and some form of collagen disease. Laboratory investigations failed to confirm any of these possibilities.

The combination of this clinical syndrome and the radiological changes suggested pulmonary fibrosis, possibly the Hamman-Rich syndrome. Lung biopsy was then performed, and histological examination was consistent with the diagnosis. Identification of the pathological changes may at times be difficult, one case having been initially diagnosed as metastatic adenocarcinoma because of the pseudoglandular appearance (Rubin and Lubliner, 1957).

In the early cases, treatment consisted of measures for cardiac failure, chemotherapy for terminal infection and oxygen administration. This treatment failed to halt the process, but some patients survived for several months.

Adrenal steroids and "Corticotrophin" are known to inhibit fibroblastic activity, and their successful use in other forms of pulmonary fibrosis, such as sarcoidosis, prompted their trial in this disease. The aim of treatment is to inhibit fibroblastic activity in the early stages, thus preventing irreversible interstitial fibrosis. If, as has been suggested, a hypersensitivity reaction is involved, again steroids should be beneficial.

At least 20 patients have now been treated with adrenal steroids, but results have been variable. Failures with steroid therapy appear to be due to three main causes: (i) treatment delayed until advanced stages of the disease, with marked irreversible fibrosis, have already occurred; (ii) early discontinuance of therapy; (iii) inadequate dosage of steroids. These are illustrated to some extent by the various cases reported.

Two of the earlier patients treated with steroids by Rubin *et alii* and by Cox and Kohl had long histories before institution of therapy, and advanced disease was found at autopsy. Recently, Carabasi has reported two similar cases in which late steroid therapy was attempted. No improvement was noted in these cases, suggesting that successful treatment of the disease may only be expected when it is begun in the early stages. Early diagnosis, however, may be difficult in view of the insidious onset of symptoms, so that a timely lung biopsy may alter a poor prognosis for patients with pulmonary disease suggesting this syndrome.

Even in cases with symptoms of long duration, the disease process may not have reached an irreversible stage. The following cases suggest that a trial of steroids is warranted in spite of a long history.

Van Slyck described a case of a woman, aged 57 years, who was treated with ACTH and prednisolone 21 months after the onset of her symptoms. Her cyanosis and dyspnœa were relieved, but clinical and radiological signs in her chest remained unchanged. Tuft and Girsh record the case of a woman, aged 44 years, who had an approximately 18 months' history before steroid therapy was started. After maintenance on 20 mg. of prednisone daily for 14 months she had gained weight and her dyspnœa had decreased, demonstrating that even in cases with fairly long-standing disease life can be maintained on steroid therapy. Freedman and Deaton have similarly maintained on steroids for three years a man with advanced disease, aged 55 years. Partial improvement such as this may be ascribed to the varying stages of the disease process in different parts of the lung.

The rate of progress of the disease process may vary considerably, so that "acute" and "chronic" forms of this condition have been suggested. This is illustrated to some extent by the variable results with steroid therapy in the following two cases.

Harris *et alii* describe the case of a woman, aged 61 years, with an onset of symptoms seven months before treatment, in whom early clinical improvement occurred, but no radiological improvement was evident. She died two and a half years later despite continuous cortisone treatment, and at autopsy was found to have advanced stages of the disease. Hoff described the case of a man, aged 30 years, who had a history of progressive dyspnœa and cough for five years; he had been maintained on prednisone for 14 months with clinical but minimal radiological improvement.

Peabody *et alii*, Schechter and Wildberger and Barclay describe cases in which initial improvement occurred with steroids, but rapid deterioration and death followed

withdrawal of hormones, despite reinstitution of ACTH and cortisone in massive doses. In these cases, the adrenal glands were normal at autopsy, and failure of prompt treatment with ACTH and cortisone makes pituitary suppression unlikely. A similar exacerbation of symptoms has been noted on cessation of steroid therapy in the treatment of beryllíosis and silicosis. The reason for this "escape phenomenon" is not known. These authors concluded that once steroid therapy is instituted it should be permanent. The danger of sudden death in this syndrome outweighs the hazards of long-term steroids.

Already several patients have been successfully treated with steroid therapy. In 1956, Pinney and Harris described the case of a woman, aged 27 years, who was treated with cortisone approximately seven months after the onset of symptoms. Marked clinical improvement occurred, and after eight and a half months' continuous steroid therapy, she could carry on with relatively normal activities, and an X-ray film of her chest was virtually clear. This patient was still living after 17 months.

Fleishman *et alii* describe the case of a woman, aged 21 years, who was maintained in satisfactory health for over three years. Treatment with steroids was begun on the presumptive diagnosis of the Hamman-Rich syndrome because the patient was critically ill. Later the diagnosis was confirmed by lung biopsy. This case was also noteworthy because several attempts were made to discontinue treatment. At the last attempt the patient was quite well for seven months before her symptoms recurred.

Initial doses of cortisone (or its equivalent) should be high. A dosage of 200 to 300 mg. of cortisone (or its equivalent) seems advisable in the initial stages. This is illustrated by comparison of these successful cases with the case described by Callahan *et alii*, of a patient who died 27 days after treatment with small doses of ACTH. In cases of undiagnosed pulmonary fibrosis the danger of reactivating a dormant tuberculosis focus with steroid therapy is a factor which could be obviated by suitable investigation and the use of anti-tuberculosis drugs if necessary.

The ætiology of the Hamman-Rich syndrome is unknown. Hamman and Rich suggested that the disease might be due to a virus infection. Similar interstitial changes have been found in scrub typhus and in virus pneumonias of various types, but as yet, no viral agent has been isolated.

Hypersensitivity has been suggested because similar changes occur after the administration of hydrallazine and hexamethonium in the treatment of hypertension. Read has produced similar changes to the Hamman-Rich syndrome in rats, by the intratracheal injection of rabbit anti-rat-lung serum. This concept may explain why so many diverse conditions can produce the same pathological picture.

Interstitial pneumonitis occurs in rheumatoid arthritis and in other collagen diseases, especially scleroderma, and it has been suggested that this disease may be a collagen disease.

The case described in this report illustrates the desirability of early lung biopsy to establish the diagnosis, and also the likelihood of a favourable response to steroids in adequate and prolonged dosage.

Summary.

1. A case of diffuse interstitial fibrosis of the lungs (Hamman-Rich syndrome) is presented.

2. The case was diagnosed by lung biopsy, approximately three months after the onset of symptoms. After nine and a half months of continuous steroid therapy, the patient, a woman aged 37 years, is now enjoying full activities and has a virtually clear skiagram of the chest.

3. A brief review of this syndrome, with emphasis on early diagnosis and prolonged treatment with steroids, is included.

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Addendum.

On May 7, 1959, the patient described in this report gave birth to a normal living male child, birth weight 6 lb. 5 oz. Her labour and post-partum convalescence were quite normal. She now weighs 158 lb. and has no respiratory symptoms at all. Prednisolone (15 mg. daily) has been administered continuously for approximately 14 months.

ULCERATIVE COLITIS ENDING IN POLYPOSIS COLI.

By GODFREY HARRIS,
Sydney.

First Episode, 1950: Psychotherapy.

AN intelligent, single woman of twenty-four in that enterologically remote year, 1950, after six months of increasing diarrhœa, spent seven desperate months in hospital with the electrolytic imbalance and cachexia of ulcerative colitis. In those days neither physicians nor surgeons hesitated—they passed the fundamental problem over to the psychiatrists, who set to work undaunted on a typical "psychosomatic" problem (unfortunately the very word "psychosomatic" makes me flinch). They relied, perhaps unwittingly, on the usual psychiatric triad, i.e., a former New South Wales public school teacher and writer of best-sellers, Dr. Havelock Ellis, F.R.C.P., and Professor S. Freud, another literary gentleman with an interest in the effect of sex on misunderstood ancient history, and also, no doubt, their own libido. With this extraordinary equipment (I myself prefer a microscope), instead of investigating the deterioration of their patient's colonic mucosa, the psychiatrists plunged into the patient's subconscious and netted two or three astounding birds for their psychopathological aviary. These Freudian fowl, they alleged, had destroyed the lining of the patient's large intestine. The young woman apparently recovered completely, as such people often do even without adequate nursing, and she married.

Second Episode, 1954: Antibiotics.

In 1954 the patient's health began to deteriorate again, and she had two months in hospital with the bloody flux, tenesmus and anorexia; there she was treated, this time with the intestinal bacteriostatic "of choice", sulphasuxidine, by both available routes.

Whether the imaginary bacteria of her ulcerative colitis were more susceptible to antibiotics than the imaginary Freudian horrors had been to the blandishments of psychiatrists, I cannot decide. At any rate, she again became free of symptoms, happy, cheerful and self-possessed after only eight weeks in hospital. Her first child was born in 1955 and her second in 1957 without any colonic protest.

Third Episode, 1958: Corticoids.

In April, 1958, bloody diarrhœa recurred, and sigmoidoscopic examination revealed the startling appearance of confluent ecchymoses, more familiar to me in victims of hæmolytic snake venom. I saw no polypi in her rectum.

The year 1950, I have emphasized, was enterologically remote—well before the advent of Hench's corticoids and the popularization of colectomy by the neo-Aztecs of Birmingham. The drug-house peddlers now have at least 57 competitive varieties of corticoids to offer for her treatment, each, of course, therapeutically superior to the others. The rationale of the treatment I do not know; its dangers I fully appreciate. Prednisone controlled the bleeding, and in fact the patient became chronically constipated, an odd complication. In May she was fit to be examined radiologically.

Polyposis Coli.

The disordered state of the lining of the patient's large intestine was demonstrated excellently by a temporarily adherent film of barium sulphate in the lumen of the air-filled colon. Fantastic disorganization of the bowel lining after eight years of ulcerative colitis is shown superbly as mucosal wrack. This "polyposis coli" with myriads of redundant tags projecting into the lumen of the bowel, its mucosa a thing of shreds and tatters, is the penultimate lesion of ulcerative colitis. The ultimate lesion is, of course, carcinoma.

Haustral Pattern: A Criticism of Accepted Theory.

The other films without air contrast show haustration (i) present and (ii) absent in the same colon on the same day. If we note carefully the timing of the pictures illustrating this condition—first, a short, narrow, low colon without haustration with both hepatic and splenic flexures at the level of the fifth lumbar vertebra; secondly, a larger, wider, higher colon with haustration and the flexures at the level of the second lumbar vertebra; and thirdly, the picture showing the colon at its largest, widest and highest, taken last of all—we must appreciate that Brookes, whose monograph "Ulcerative Colitis and its Surgical Treatment" stands like the shadow of a great rock in a weary land, has in this respect been misled. He states: "At first the colon loses haustration so that it presents a smooth outline . . . As the disease progresses the colon becomes narrowed and diminished in length . . . ." It is apparent from the pictures of this series that no reliance as to the stage of the disease can be placed on the length or width of the colon or on the absence of haustral pattern, which can and does alter radically from minute to minute under load.

Final Treatment.

To reemphasize the changes in the treatment of ulcerative colitis which the last decade has seen, there are (i) the concept of the biochemical lesion in the pathology of chronic inflammation, (ii) the use of cortical steroids in practical clinical medicine for lesions of this sort, and (iii) the advocacy of total removal of the large intestine to save the patient from relapse and, more particularly, from malignant disease. The effect of the *bouleversement* in the theory of the pathology has led, in Robb-Smith's words, "to a change in bacteriological thought, so that toxins have ceased to be regarded as traumatological poisons but as specific metabolic products to be defined by their action both chemical and pathological". In attempting to understand this explanation we may recall Madame de Diffand's reply to Cardinal Polignac, when he told her that St. Denis, after his execution, carried his severed head from the headsman's block in Montmartre to the Abbey which bears his name, "Ah, Monseignor", replied the Marquise, "in such circumstances it is only the first step that counts." The treatment of non-bacterial inflammation by cortical steroids is a mystery to me; but so also is the biochemistry of non-bacterial inflammation. Their efficacy, however, is beyond dispute.

As for the drastic surgical intervention, it was not until 1954 that Brookes could claim in his monograph "the advantage of removing the whole large bowel in a single procedure following ileostomy is obvious". Nothing short of a study of his statistics can adequately express the case for such drastic operative treatment; indeed, Sir Heneage Ogilvie in 1940 had written: "The surgery of ulcerative colitis is essentially destructive. It comes in where medicine has failed and has no place as an adjunct to medical treatment."

Ulcerative Colitis, Ileo-Colitis and Procto-Sigmoiditis.

Finally, the X-ray picture showing morphological changes at the ileo-caecal junction in a patient with advanced regional ileitis helps to show the distinction between this disease and ulcerative colitis in a very striking way. Proctosigmoiditis (not illustrated radiologically because it is so easily seen by rectal speculum and sigmoidoscope) is so evidently a separate entity that one wonders why Brookes's case for the separation of the three anatomically distinct types of non-bacterial colitis has not yet been universally accepted.

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I am particularly indebted to Dr. John Ryan for the air-contrast radiography, and to Dr. B. P. Anderson Stuart for the radiological demonstration of the changes in the position and morphological appearances of the patient's colon, and to Dr. H. Freilich for the demonstration in another of my cases of the "string-lesion" or regional ileitis with ileo-colitis.

Reviews.

Diseases of the Nervous System: Described for Practitioners and Students. By Sir Francis Walshe, M.D., D.Sc., F.R.S., with chapters on "The Neurological Complications of Liver Disease" and "Hepatolenticular Degeneration", by J. M. Walshe, M.R.C.P.; 1958. Ninth Edition. Edinburgh and London: E. and S. Livingstone, Limited. 9½" × 5¾", pp. 392, with 60 illustrations. Price: 30s. (English).

WHEN we received a copy of the ninth edition of this book, we turned to a first edition in our possession for comparison. As a measure of his distinction as a neurologist, the author, F. M. R. Walshe, is now Sir Francis, and a Fellowship of the Royal Society marks his scientific status.

The first edition, published only eighteen years ago, has 274 pages of text, while the present contains nearly 100 more. In the preface to the first edition the writer defined his aim: to produce a book of use to students and practitioners, to avoid the temptation "to mention, however briefly and uselessly, something of everything" which besets so many authors, since few are willing "to face the imagined reproach that they have left out something new, rare, or ingenious". He avoids "the tyranny of words" which "stifles thought in terminology", and he does not create "a carnival of literary expansiveness". That he avoided these errors is now a noteworthy part of medical history.

With each new edition valuable advances have been recorded, and, where necessary, current trends are subjected to critical evaluation. The present enthusiasm for cervical osteoarthrosis is apparently not shared by the author, and caution is urged in accepting the carpal tunnel syndrome as the cause of acroparæsthesiæ. The new edition continues to reflect "many advances in due proportion", but "within the limits defined by the first edition". There are, however, two exceptions, and very interesting they are. They deal with the neurological complications of liver disease and hepatolenticular degeneration, and are written by J. M. Walshe, Assistant Director of Medical Research at Cambridge University and son of the major author. These apparent exceptions are not due to Sir Francis's essential warmth of heart, for they reveal principles which will be the basis of further expansions of knowledge, and which unite general medicine and neurology. We learn that hepatic coma may be precipitated in cirrhosis of the liver by injudicious treatment—for example, the use of ammonium ion exchange resins, "Diamox", injudicious paracentesis and the use of hypnotics. It is of particular interest that these brief chapters are well written and concise, with a lucidity comparable to the father's.

References to treatment indicate the sound common sense which underlies the whole presentation. The student and practitioner will not find a list of all the things which have ever been done to, or recommended for, the patient. Only therapy of proven value is mentioned, and a chapter entitled "Some General Observations upon the Treatment of Nervous Diseases" will satisfy those who hope to combine the science and art of medicine with morality in their work.

Words do not exert a tyranny over their master, and many of Sir Francis's sayings are treasured by his students. Although they are barbed, there is sound common sense behind them. "If he [the doctor] cannot increase his patient's expectation of life, he can, at least, refrain from being a bird of ill-omen and a cutter-off of those creature comforts and relatively harmless habits which have become part of the life of the patient and are thus so much dearer to the old man than the young." He condemns "the so-called relaxations which make a toil of pleasure by the man's competitive spirit and his egotism".

It may be thought in some instances that treatment is dismissed too briefly, as in myasthenia gravis; but it may truly be said that this condition should be treated only by an expert. Similarly, perspective in investigation is enjoined:

> In epilepsy the interpretation of the electoencephalogram is a skill founded upon experience and exercised in close correlation with the clinical history and state of the patient. The interpretation is not free from a subjective element, and should not be regarded as a simple affair, infallibly providing a diagnosis in every instance . . . if realization of this [its true use] spreads we may hope that it will lead to a less widespread and undiscriminating demand for the electroencephalogram.

It is hoped that this review will suggest that the book is one to be on all medical shelves—and the price is only 30s. sterling.

Practical Cardiology. By Albert Salisbury Hyman, M.D., F.A.C.P., F.A.C.C.; 1958. New York: Landsberger (Medical Books), Inc. 8" × 5", pp. 322. Price: $7.00.

THE author states that this book is intended to be "of service to the busy general practitioner". It begins well with some excellent commonsense advice on history taking and physical examination, although one might make the minor criticism that the material would be of more practical benefit to the busy general practitioner if it was presented more concisely. However, the chapter on heart sounds and murmurs contains many statements which are incompatible with modern cardiological knowledge. For instance, few cardiologists would agree with the statement that a systolic murmur which "is not accompanied by accentuation of the first sound at the apex and has an increase in the loudness of the second pulmonic sound . . . is functional", or that "functional murmurs" are due to poor tonus of the cardiac muscle allowing relaxation of the atrioventricular ring, and that deep respiratory exercise causing improvement in heart-muscle tonus will abolish the murmur. Another unorthodox contention is that a patient with a blood pressure of 240/20 mm. of mercury and a mean pressure of 93 has a much brighter prognosis than another man with a pressure of 180/110 mm. of mercury and a mean pressure of 143.

It is regretted that this book cannot be recommended to general practitioners and students because of the many misleading and inaccurate statements, such as those mentioned above, which are included in much useful and practical material.

Clinical Hæmatology in Medical Practice. By G. C. de Gruchy, M.D., F.R.A.C.P., M.R.C.P. (Lond.), M.C.P.A., with a foreword by J. V. Dacie; 1958. Oxford: Blackwell Scientific Publications. 8¾" × 5½", pp. 632, with many illustrations. Price: 50s. (English).

IN every specialty of medicine there are one or two reference books which are well recognized by all who work or practise in the specialty. Many editions have usually been published, and inevitably as knowledge has advanced the size of the book and the detail included have increased. The result is a large, well-documented book, more useful for the established specialist than for the general physician or general practitioner. Hæmatology has followed this pattern, and undoubtedly the time has arrived for an entirely new book, written for the non-specialist, and with the problems presented by patients as the prime consideration. Dr. de Gruchy's book supplies this need, and must be in the hands of all general physicians, hæmatologists, post-graduate students and laboratory workers. It will also be useful for the general practitioner who wishes to investigate and treat logically his patients suffering from blood disorders. He will find the author's writing lucid, logical and interesting, and based on practical experience of patients.

One of Dr. de Gruchy's problems must have been what to include and what to omit, and his decisions have resulted in a book of 620 pages, including the index. He possibly tried to complete his task in less space, but the book is well balanced, the common disorders receiving the greatest attention. The reader need not fear emphasis of oddities. The first two chapters are devoted to a description of the blood cells and bone marrow, and a general discussion of the nature, causation, clinical effects and invesigations of anæmia. Five chapters concern the anæmias and two the physiological and pathological variations of the white cells, leucopenia and the leukæmias. Polycythæmia, myeloscleroșis, tumours of the lymphoid tissue and hypersplenism receive attention in the next three chapters, whilst the last three are devoted to the hæmorrhagic disorders, disorders of pigment metabolism, the blood groups and blood transfusion.

The author's wide experience both in the laboratory and in the ward is evident throughout, and he has rightly stressed the investigation and management of patients. At the same time he has summarized the recent and often complex developments that have occurred, for example, in blood coagulation, abnormal hæmoglobins, vitamin B_{12} metabolism and Rh blood groups, so that clinicians need no longer be confused and overawed by their laboratory colleagues.

Reading is facilitated by tables, line drawings and photographs of blood films, and each chapter concludes with a list of useful references, the most important of which are printed in bold type. The format of the book is similar to that of a large series of medical monographs recently published by the house of Blackwell, and the book itself is characterized by a negligible number of printing errors. It is the first book on clinical hæmatology written by an Australian physician, and it can be recommended without reservations to all Australian medical practitioners who seek to widen their knowledge of this fascinating branch of medicine.

Etiology and Treatment of Leukæmia: Proceedings of the First Louisiana Cancer Conference. Edited by Walter J. Burdette, Ph.D., M.D., F.A.C.S.; 1958. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical), Limited. 9¼" × 6¼", pp. 167, with many illustrations. Price: £2 4s.

THIS book embodies a collection of papers which were presented to the American Cancer Society in Louisiana, and introduces some of the workers in the field of leukæmia research.

The section on ætiology is deveted mainly to experimentally-induced leukæmia, and the main leukæmogens discussed here are the viruses, ionizing radiations, chemical carcinogens and œstrogens. Genetic factors which appear to determine the response of the host to these agents and the role of the thymus are presented.

Attention is directed to pitfalls in diagnosis. Accuracy in histological classification is being reemphasized, since different types of leukæmia vary in their response to different chemotherapeutic agents. Thus, in addition to conventional methods, the more frequent use of such techniques as phase-contrast microscopy and the ribonuclease test is discussed.

With regard to treatment, all the current chemotherapeutic drugs are dealt with, particularly the antimetabolites and steroids, and one paper discusses the results obtained with chlorambucil (CB1348). Problems involved in the selection of these drugs and in their dosage adjustment are apparent, but some rules are set out to help in the clinical management of these cases.

The concluding chapter presents a summary of the proceedings together with a tabulated historical survey. A valuable feature of the book is the extensive bibliography of 380 complete references, which cover most aspects of leukæmia.

Clinical Chemistry in Practical Medicine. By C. P. Stewart, D.Sc., Ph.D., and D. M. Dunlop, B.A., M.D., F.R.C.P. (Edin.), F.R.C.P. (Lond.); Fifth Edition; 1958. Edinburgh and London: E. and S. Livingstone, Limited. 8¾" × 5¼", pp. 352, with many illustrations. Price: 27s. 6d. (English).

TODAY it is a formidable task to write an excellent book on clinical biochemistry for the medical student and the practitioner of medicine; but this has been achieved by Stewart and Dunlop of Edinburgh in their fifth edition (1958) of "Clinical Chemistry in Practical Medicine". This edition has been extensively rewritten to include recent advances, such as the serum level of transaminase as a test for necrosis of the heart muscle following coronary occlusion. The importance of water and electrolyte metabolism is emphasized, and a brief description is given of the deficiency states. A lack of sodium chloride leads to lassitude, loss of appetite, muscular cramps and dizziness. Severe potassium depletion may occur in chronic renal disease, notably in the specific form of "potassium-losing nephritis". The value of paper electrophoresis in measuring plasma protein fractions in disease is described, especially in multiple myeloma, agammaglobulinæmia, nephrosis and chronic liver disease. However, the recent advances in knowledge of the protein patterns in diseases associated with abnormal immunity reactions, such as lupus erythematosus and lupoid hepatitis, will require further comment in the next edition. In the fine chapter on renal function a warning is issued that albuminuria may be absent in severe chronic renal disease. Here the urea clearance test will reveal impaired function. A section on acute tubular necrosis, which may occur in "severe shock, hypotension and dehydration", describes the cure which may be achieved in spite of anuria lasting for several weeks; the patient is sustained by carefully planned intravenous infusion and perhaps by dialysis of the blood by means of the artificial kidney. Other chapters cover gastric, hepatic and pancreatic function. The endocrine glands receive their due, but too much emphasis is placed on the basal metabolic rate as a measure of thyroid function. It is pleasing to note that I^{131} and protein-bound iodine have entered the lists.

This is a splendid book, wisely planned to help and encourage both student and practitioner. Specialists in medicine and surgery also would enjoy it.

Science News. No. 46, edited by Archie and Nan Clow. Penguin Books. 7" × 4¼", pp. 128, with many illustrations. Price: 4s. (Australia).

Science News. No. 47, edited by Archie and Nan Clow; 1958. Mitcham, Victoria: Penguin Books Pty. Ltd. 7" × 4", pp. 142, with illustrations. Price: 4s.

FRESH volumes of "Science News" continue to appear regularly four times a year; each of these volumes contains seven rather severely technical articles on an extreme diversity of topics of current scientific interest, with an eighth chapter entitled "Research Report", giving briefer notes on recent developments and discoveries. A few book reviews at the end of each volume, together with brief biographical notes on the contributors, are useful adjuncts. The main articles are written for the informed lay reader by specialists in their subjects, and can be read by anyone with some basic scientific knowledge and a taste for this kind of mental exercise. Of medical interest, No. 46 contains an interesting article on aviation medicine, and one on new approaches to the study of bacteria, describing investigations into the nature of the bacterial cell. Among the other articles, the theoretical and practical aspects of the newer physics are well represented, with titles such as "The Twilight of Parity Conservation" (opening with a discussion of the quantum theory), and "The Orbit of a Satellite" (describing a method of calculating the same).

In No. 47 we find an article on psychopharmacology, describing recent advances in the discovery of drugs which control mood and behaviour, and one on œstrogens and their metabolism, which is essentially a biochemical essay. Another article deals with the application of information theory and probability models to experimental psychology. Of good general interest is an article on the structure of the interior of the earth, which gives the background of what one part of the International Geophysical Year activities were about.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Glaucoma: Transactions of the Third Conference, January 8, 9, and 10, 1958, Princeton, N.J.", edited by Frank W. Newell, M.D.; 1959. New York: Josiah Macy, Jr. Foundation. 9" × 6", pp. 272, with 73 figures and 21 tables. Price: $5.25.

Contains papers and discussions on tonography, osmotic factors in the formation of aqueous humour, consensual changes in intraocular pressure under experimental conditions and tonography in the clinical management of glaucoma.

"Long-Term Prognosis in Pulmonary Tuberculosis Detected by Mass Radiography: A Country-Wide Survey with Controls and a Comparison Between Two Mass Surveys with a Seven-Year Interval", by Ivar Källqvist, *Acta Tuberculosea Scandinavica* (Supplementum 44; 1958). Copenhagen: Ejnar Munksgaard. 9¼" × 6¼", pp. 178, with illustrations. Price: not stated.

The findings from a Swedish survey.

"Babies Without Tears: A Mother's Experiences of the Lamaze Method of Painless Childbirth", by Marjorie Karmel; 1959. London: Secker & Warburg. 7¼" × 4¾", pp. 208. Price: 15s. 6d. (English).

The Lamaze method is described as an adaptation of methods based on the work of Pavlov.

The Medical Journal of Australia

SATURDAY, JULY 18, 1959.

INACTIVATED AND LIVE POLIOVIRUS VACCINES.

WITH all infectious diseases prevention is better than cure. This is particularly true of viral infections, for which no specific therapy has been developed, except perhaps the prophylactic use of gamma globulin in measles and infectious hepatitis. Australia's geographical isolation makes quarantine an effective method of keeping out some of the major human viral infections (smallpox, yellow fever, rabies) as well as many which are of great importance to our livestock industries. But we are constantly exposed to the risk of infection with a large number of other viruses, of which the most important are probably influenza, infectious hepatitis, poliomyelitis and the common exanthemata of childhood. Of these, poliomyelitis has long provoked the most acute public fear. Prevention of these diseases can best be effected by specific immunization against them, and all will be aware of the success which has followed the introduction of the Salk-type formalin-inactivated poliovirus vaccine a few years ago.

The use of an inactivated viral vaccine is something of a novelty. All veterinary viral vaccines, and the other important human viral vaccines, are attenuated living agents—exemplified by vaccinia virus and 17D yellow fever virus vaccine. In poliomyelitis also there have been, concurrently with and since Salk's introduction of a killed vaccine, intensive investigations of the possibilities of living attenuated vaccines for poliomyelitis. The two principal investigators have been A. B. Sabin and H. Koprowski. In the course of this work a great deal has been found out about the variations in virulence which can occur in poliovirus strains during laboratory manipulations, and several attenuated strains of each poliovirus type are now available. From these Sabin[1] has selected three strains which have very low neurovirulence, yet multiply well in the cells of the alimentary tract. The advantages claimed for the live vaccines are that they can be administered orally, that relatively small amounts of vaccine suffice, so that production problems are simplified, and, according to Sabin, that the immune response following infection with an attenuated live vaccine is superior in type as well as in intensity to that produced by formalinized virus. A disadvantage is that all three poliovirus types have to be given separately, for the development of intestinal infection with one type interferes with the establishment of infection by other types. Sabin suggests that interference can be avoided by feeding the three types of virus at intervals of not less than three weeks, in the following order: type 1, then type 3 and finally type 2.

A number of investigators have now carried out intensive studies with attenuated living virus strains with the object of obtaining detailed information on the pathogenesis of infections due to the attenuated vaccines in completely susceptible, in Salk-vaccinated and in naturally immune individuals. One important difference between the immunity following the use of live vaccine and that following the use of formalinized vaccine seems to be that, whereas infection of the alimentary tract and dissemination of virus appear to be unaffected by vaccination with Salk-type vaccine, live vaccines appear to limit greatly the subsequent multiplication of virulent viruses in the cells of the gut. Thus widespread use of live vaccines might greatly interfere with the dissemination of naturally occurring virulent polioviruses in the community. The all-important question, of course, is the safety of attenuated live poliovirus vaccines, and this is a question which can be resolved only by field trials on ever-increasing numbers of people. Such trials have in fact been recommended recently by the Expert Committee on Poliomyelitis of the World Health Organization.[1]

There is an important point of difference between live poliovirus vaccine and most other living vaccines used in human and veterinary medicine. Most live viral vaccines are given by an "unnatural" route, which minimizes the risk of spread of the virus to susceptible individuals: secondary cases of vaccinia, for instance, are rare and are usually associated with prior skin disease. Live poliovirus vaccines, on the other hand, are administered orally, that is, by the natural infection route, and they are excreted in the fæces and can certainly spread to individuals other than those vaccinated. Experiments in human volunteers by Sabin himself, by Dick and Dane, and by others, have shown not only that attenuated viruses which multiply in the cells of the intestinal tract will spread from vaccinated to susceptible individuals, but that a limited degree of increased neurotropism sometimes occurs. This underlines the necessity for the careful selection of virus strains of very low neuropathogenicity, as judged by the most sensitive available tests, and for extensive field trials. The results of one such trial have now been reported.[2] In the latter half of 1958 and early this year there was a type 1 poliomyelitis epidemic in Singapore. It is generally held that in previously unvaccinated individuals immunity is produced too slowly by formalinized vaccines for these to be of any use in the presence of epidemic poliomyelitis, whereas live vaccines act more rapidly and, as explained below, may also have an "interfering" effect. About half a million children between three months and ten years of age were at risk, and of these 200,000 were given an oral dose of type 2 vaccine, Sabin's recommended strain being used. Type 2 was chosen because possible cases

[1] *Brit. Med. J.*, 1959, 1: 663 (March 14).

[1] *World Health Organization Technical Report Series*, 1958, No. 145.

[2] *Brit. Med. J.*, 1959, 1: 1541 (June 20).

of paralysis due to the vaccine could be recognized, and because of evidence accumulated by Sabin that the presence of type 2 virus in the gut interferes with natural infection by other polioviruses. In addition, heterotypic immunity is thought to afford a slight degree of protection. Six of the 200,000 vaccinated children developed paralysis due to type 1 virus, and in the same period of time there were 179 cases in the 300,000 non-vaccinated children of the same age group. One case of type 2 paralytic poliomyelitis developed in a non-vaccinated child, and this was thought to be due to a "wild" virulent type 2 strain, as these were circulating in a neighbouring community. Some of the virus strains isolated from those vaccinated showed slight increases in neurovirulence, as judged by the sensitive monkey intraspinal test, but this did not appear to be progressive, so far as could be judged by tests made of type 2 strains recovered from contacts of the vaccinated children.

Studies such as this Singapore trial will obviously encourage authorities in lesser developed communities, where nevertheless improving hygiene is increasing the paralytic poliomyelitis risk, to contemplate vaccination with live attenuated strains. They do not suggest that Australia should do so. We are fortunate in having available in Australia a formalinized vaccine of high quality, as regards both its safety and its immunogenic potency; and the dramatic reduction in the incidence of paralytic poliomyelitis following its use in Australia is known to all practitioners. Of course, the last word in killed poliovirus vaccines has not yet been said. Increasing information on the physical structure of poliovirus gives promise of the ultimate manufacture of a vaccine of the antigenic protein only—something comparable perhaps with diphtheria and tetanus toxoids. Public health authorities in the U.S.A.[1] are now pressing for the inclusion of poliovirus vaccines with tetanus and diphtheria toxoids and pertussis vaccine in a "quadruple vaccine", and the possibility of producing this for use in Australia was discussed at the last meeting of the National Health and Medical Research Council. We are in the fortunate position of being able to await further developments in live virus vaccines secure in the knowledge that, if the available formalinized vaccines continue to be properly used, the Australian population can be effectively protected from paralytic poliomyelitis.

The implications of the current intensive investigations of poliovirus vaccines are not, of course, limited to poliomyelitis prevention. Since chemotherapy of viral infections will never attain the importance of the drug treatment of bacterial diseases, owing to the intrinsic nature of viruses, we must rely on immunological methods of protection. The rapid advances in virology over the last few years have made vaccines for measles and adenovirus infections practical possibilities, and hepatitis virus can not resist our efforts to cultivate it for ever. The controversy, killed vaccine versus live attenuated virus vaccine, now current with poliovirus, may well crop up in the near future with several other human viruses—measles, infectious hepatitis—and perhaps, once again, with influenza.

[1] *Am. J. publ. Hlth*, 1959, 49: 644, 678 (May).

Current Comment.

BILLROTH I AND BILLROTH II.

THE history of gastrectomy has seen many changes in fashion among the several types of operation and their modifications which have been proposed from time to time, and experience has revealed drawbacks and pitfalls in all of them; so the search for the operation of choice still goes on, influenced by improvements in operative techniques and by the experience and preferences of individual surgeons. J. L. Herrington[1] has recently published the results of an extended comparison of the Billroth I and Billroth II types of reconstruction after gastric resection. He points out that the Billroth I type of reconstruction enjoyed a brief period of popularity after its introduction in 1881. The procedure was then abandoned because of technical difficulties and post-operative complications. However, during the past 15 years or so, the Billroth I operation has come back into popularity, and there exists now considerable divergence of opinion in regard to the relative merits of the two types of Billroth reconstruction.

Herrington's study consists of a clinical evaluation of the results of operation in two groups of patients with benign gastric and duodenal ulcer disease. One group underwent the Billroth I operation, and the other was subjected to a conventional Billroth II type of reconstruction or one of its modifications. In addition, bilateral subdiaphragmatic vagotomy was performed on all patients with duodenal ulceration in both groups. As a result of this study, Herrington tries to determine the relative indications for the selection of either the Billroth I or the Billroth II reconstruction for any particular patient with benign gastric or duodenal ulceration.

The Billroth I group consisted of a total of 107 patients with a post-operative follow-up study ranging from six months to three-and-a-half years. Of this number 98 were operated on for duodenal ulcer and nine for benign gastric ulcer. The Billroth II series comprised a total of 209 patients followed for periods ranging from six months to eleven and a half years. Of these, 196 patients were suffering from complications of duodenal ulcer and 13 patients had benign gastric ulcer. The two groups were comparable as regards age and sex distribution.

Among the 107 patients undergoing a Billroth I reconstruction there were three hospital deaths, and in the Billroth II group there were eight deaths among the 209 patients. It is stated that none of the three deaths after the Billroth I type of reconstruction were directly attributable to a technical difficulty resulting from the operation, and among the eight deaths after the Billroth II reconstruction, only one was due to a technical error in the performance of the operation, namely, stomal obstruction. The incidence of significant post-operative complications was 19% in both groups. In the Billroth I group, obstruction at the gastro-duodenostomy stoma was the most frequently encountered complication resulting from a technical fault; this occurred in seven patients during the post-operative period and necessitated a second operation in five of these. Among those who underwent Billroth II reconstruction, eight patients developed stomal obstruction, but in five of these gastric suction was successful in alleviating the obstruction; stomal revision became necessary in two others, and one patient succumbed. Other serious complications were post-operative hæmorrhage (three cases in the Billroth I group and two in the Billroth II group) and leakage (one case of leakage at the anastomotic site in the Billroth I group and three of leakage from the duodenal stump in the Billroth II group).

As regards the subsequent course of these patients, Herrington notes that few patients in either group lost

[1] *Surgery*, 1958, 44: 1040 (December).

weight after the operation. He attributes this to the combination of vagotomy and a conservative degree of gastric resection. Symptoms suggestive of the dumping syndrome were noted in 23% of the patients in the Billroth I group, but they were mild in three-quarters of these, and in most cases disappeared after some weeks or months. In the Billroth II group, the over-all incidence of dumping was 37%, which was mild in two-thirds of these patients and severe in only five; for two of these five patients a second operation became necessary, and the reconstruction was converted from Billroth II type to Billroth I, with satisfactory results in both cases. The period of follow up in the Billroth I group was too short to judge recurrence rates, but at the time of writing of Herrington's paper only one recurrence had been noted in this group—a large ulcer in the posterior wall just distal to the gastro-duodenostomy. In the Billroth II group there had been no recurrence among 180 patients who had undergone vagotomy and antral resection for duodenal ulcer, and one recurrence among the 13 who had undergone resection for a gastric ulcer.

In his evaluation of the final results, Herrington states that in the Billroth I group 80 patients (76%) obtained an excellent result from their operation, and 17 were classified as having obtained a good result with minimal post-operative complaints. Six were improved, but the result was classed as only fair, and for two the result was poor. In the Billroth II group, 64% had remained symptom-free, 26% had obtained a good result, in 7% the result was graded as fair, in 3% (seven patients) the result was poor, and in four patients the operation was a complete failure; it was observed that although women made up only one-sixth of the whole group, all the failures and half of the results in which the outcome was only fair were in female patients.

The results in these two groups are thus seen to be very similar. The difference in mortality is not significant, and the incidence of complications is identical. The total of results classified as excellent and good is approximately the same in each group, though a somewhat larger proportion of patients remained completely free of symptoms after their operation in the Billroth I group. Symptoms of the dumping syndrome occurred more frequently in the Billroth II group, and this is stated to be in accord with experience elsewhere. Harrington considers that the Billroth I reconstruction combined with vagotomy and antral resection has so far given slightly better results in the surgical management of duodenal ulceration, though he points out that it is too early to be sure of the recurrence rate. He therefore prefers the Billroth I reconstruction in most instances where the duodenal ulcer can be removed safely and without difficulty, especially in underweight individuals and in females. However, he considers that the procedure is definitely contraindicated for patients with a large posterior-wall duodenal ulcer which cannot be safely or completely removed, especially in obese individuals, and that for such patients the Billroth II reconstruction is better. He also prefers this procedure for large, obese patients generally.

TWELFTH WORLD HEALTH ASSEMBLY.

THE Twelfth World Health Assembly opened in Geneva on May 12 and ended on May 29, 1959. The chairman was Sir John Charles, Chief Medical Officer, Ministry of Health, United Kingdom. The three-week session was attended by delegates from 82 of the 90 member and associate member States of the World Health Organization, including those from two new members, Columbia and Guinea. The United Nations and specialized agencies, as well as non-governmental organizations interested in health matters, sent observers to the meeting.

The World Health Assembly adopted the programme of work for 1960 along with a regular budget of $16,918,700. Activities planned include the control of major communicable diseases such as tuberculosis and leprosy, and eradication campaigns against malaria and smallpox. Expansion of work and research in the field of virus disease, nutrition and health statistics is included in the programme, as well as continuation of WHO activities in such traditional fields as quarantine, standardization of drugs, education and training of health personnel, and exchange of information.

Three topics receiving particular attention were medical research, water supply and smallpox eradication. WHO is to enlarge considerably its activities in medical research to fill the gaps in coordination and communication between research workers throughout the world. The main emphasis will be on unsolved problems of importance for the advance of public health, including the conquest of communicable disease. Particular attention will be paid to the investigation of factors contributing to the incidence of heart disease and cancer. The Assembly included a sum of $500,000 in the 1960 budget for this programme, and created a special account to receive contributions for international research work. On the question of water supply the Assembly recommended that countries give priority to the provision of safe and adequate water supplies to their populations and mobilize all their resources to contribute to this end. WHO is to provide leadership in a coordinated global programme of community water supply, and to provide technical and advisory services when so requested by governments. The Assembly stressed that safe and adequate water supplies are essential to the protection and improvement of health and are indispensable for economic and social development. The question of smallpox eradication is now receiving serious attention. Within the past three years, 56 countries and territories have suffered epidemics of smallpox, a lethal disease which can nevertheless be eradicated by continuing mass vaccination of the population until no further cases occur. The Assembly asked for intensive campaigns to rid the world of this dangerous, disfiguring and expensive disease, the answer to which has been known for more than a century and a half.

Another important programme of the World Health Organization, malaria eradication, was examined by the Assembly, which noted with satisfaction that the work was progressing well, but that funds were lacking to finance WHO's continuing leadership in this global campaign. Governments, industry, foundations and others were urged to join with WHO in eradicating malaria by contributing to the World Malaria Fund.

Other decisions taken by the Assembly included enlarging the membership of the WHO Executive Board from 18 to 24. For this constitutional change to become effective, it has to be formally ratified by two-thirds of WHO member States. It was resolved to postpone until next year the decision on a proposal that WHO organize an International Health and Medical Research Year. On this matter, it was pointed out in the Assembly that there was already a heavy commitment of national and international effort; WHO has only recently embarked on an extensive and intensive programme embodying practical steps to combat widely prevalent diseases such as malaria, tuberculosis, smallpox and leprosy, which will involve active international cooperation and exchange of knowledge and experience in these diseases, as well as cholera, cancer, cardio-vascular ailments and poliomyelitis. Planning of a new headquarters building to house WHO in Geneva was also authorized by the Assembly, which accepted the generous offer of Swiss and Genevese authorities to provide, subject to parliamentary approval, a building site and loans totalling 30,000,000 Swiss francs (United States $6,976,744). An international competition will be held for the choice of a building plan and an architect.

Dr. M. G. Candau was offered a renewal of his contract as Director-General of WHO for three years, until 1963. He is to announce his decision before November 1.

India's Health Minister invited the Assembly to meet in 1961 in New Delhi. It was decided that in 1960 the Thirteenth World Health Assembly would meet again in Geneva.

Abstracts from Medical Literature.

BIOCHEMISTRY.

Serum Albumin.

R. H. McMENAMY AND J. L. ONCLEY (*J. biol. Chem.*, December, 1958) have discovered that when amino acids are added to human plasma the only plasma protein which binds L-tryptophane appreciably is serum albumin. L-Tryptophane is bound to serum albumin predominantly at one site in a highly stereospecific manner. D-Tryptophane is bound with an affinity of about one hundredfold less than L-tryptophane. The pH dependence of binding of L-tryptophane and its analogues implies the presence of an ionizable group at the protein site which prevents binding of the small molecules when both this ionizable group and the α-amino group on the small molecule are similarly charged. Evidence is presented that the N-terminal group of the albumin is the ionizable group involved at the protein-binding site. It is apparent also that the carboxyl group of the L-tryptophane is required for binding whether it be charged or uncharged. The α-amino group of tryptophane has only a secondary role in the binding. Certain areas of the indole ring are also implicated in the binding.

Salicylate.

M. J. H. SMITH (*J. biol. Chem.*, January, 1959) has studied the oxidation of acetate-2-C^{14} and the incorporation of the radioactive carbon in the glycogen and fatty acids of the liver of the rat. Salicylate was found to increase the respiratory excretion of total CO_2 and $C^{14}O_2$, to prevent the incorporation of C^{14} into liver glycogen, and to inhibit partially the incorporation of the isotope into the liver fatty acids. The pattern of radioactivity suggested that salicylate increased the oxidation of labelled acetate and interfered with glycogen synthesis and lipogenesis in the liver.

Gaucher's Disease.

A. ROSENBERG AND E. CHARGAFF (*J. biol. Chem.*, December, 1958) state that the identity of the carbohydrate constituent of the cerebroside which accumulates in the reticuloendothelial system in Gaucher's disease is still controversial. They have isolated crystalline cerebroside preparations from the spleen of a patient with Gaucher's disease. After controlled hydrolysis the hexose was shown to be D-glucose by specific enzymic assay. Analytical values indicate that the Gaucher spleen cerebroside is essentially behenyl gluco-cerebroside.

Vitamin E.

L. M. LORWIN AND K. SCHWARZ (*J. biol. Chem.*, January, 1959) have reported an effect of vitamin E on the regulation of succinate oxidation in rat liver mitochondria. The decline in succinate oxidation in the presence of diphosphoridine nucleotide (DPN) was observed to be greater in liver mitochondria from rats deficient in vitamin E than it was in mitochondria from vitamin E-supplemented animals. The decline in the mitochondria of the deficient animals was reversed in 30 to 40 minutes after α-tocopherol was given by intraportal injection, but not by its addition *in vitro*. Sodium selenite, as a source of factor 3 in the diet, had no effect in preventing the decline. Inhibition of succinate oxidation by the accumulation of oxalacetate was strongly implicated as the cause of the decline. The necessity for DPN for the difference in decline to occur and the alleviating effect of compounds known to accelerate the removal of oxalacetate, seem to justify this conclusion. Acetyl coenzyme A, manganese ions, adenosine triphosphate (ATP) and magnesium ions were all effective in either preventing the decline or slowing its rate of occurrence. The difference in decline between the mitochondria supplemented with vitamin E and those deficient in this factor was maintained in the presence of sufficient arsenite to inhibit pyruvate, but not succinate oxidation. No correlation of these effects could be made to a difference in the activity of the reduced DPN-cytochrome *c* reductase system. The latter was not affected by the presence or absence of vitamin E in the diet.

Lens Proteins.

D. C. WOOD *et alii* (*J. biol. Chem.*, February, 1959) state that until 1955 it was rather generally accepted that there could be three soluble proteins in the lens. The authors have isolated five proteins in crystalline form from the saline extract of rabbit eye lens. It was shown that all five proteins were precipitated in quantitative yields in approximately half saturated ammonium sulphate solution. Isoelectric points, absorption spectra and sedimentation values were measured for each protein, and their relationship to previous work is discussed.

Iodine.

G. D. POTTER *et alii* (*J. biol. Chem.*, February, 1959) have shown that the mammary gland of the lactating rat is a major pathway for the elimination of iodine. As much as 50% of circulating iodide may be recovered in total mammary tissue *plus* milk in 24 hours. At six hours after the injection of I^{131} as much as 61%, and at 24 hours as much as 86% of the I^{131} in rat milk was protein bound. From 46% to 68% of the I^{131} in milk was present as protein-bound monoiodotyrosine. A small amount of protein-bound I^{131}-labelled diiodotyrosine was also found in rat milk. No other labelled compounds were detected. Injected I^{131}-thyroxine and I^{131}-triiodothyronine were shown to appear in the milk, but only in very small amounts.

Vitreous Body.

E. A. BALASZ *et alii* (*J. biol. Chem.*, February, 1959) have followed the biochemical changes in the developing cattle vitreous body (from two-month-old embryos to ten-year-old adult animals). The hyaluronic acid concentration is low in the embryo vitreous body and increases to the adult level during the first year after birth. The concentration of non-dialysable galactosamine is constant (1 to 2 mg. per 100 ml.) during the whole age range. The molar concentration of the ester sulphate present is about equivalent to that of galactosamine. The vitreous body of young embryos contains hexosamine, but very little hexuronic acid. It is suggested that most of the hexosamine belongs to fetuin, a glycoprotein also present in the α-globulin fraction of embryo and calf plasma. The electrophoretic picture of the embryo vitreous body indicates a large α-globulin fraction. The collagen concentration in the occipital part of the vitreous body is rather constant during all stages of development. The soluble protein concentration of the vitreous body does not change after birth, but it is higher in embryos. The ascorbic acid concentration increases during the pre-natal period, reaching its adult level after birth. The calcium concentration remains constant after birth, but is high during the pre-natal period. In both cases it follows the concentration in serum. The biochemical development of the vitreous body is not completed until adulthood.

Chylomicrons.

M. RODBELL *et alii* (*J. biol. Chem.*, March, 1959) have found that three proteins, A, B and C, are associated with both dog and human chylomicrons. In both species, one of these proteins, A, has been shown to have the same N-terminal amino acid, paper electrophoretic mobility and "fingerprint" pattern as does the major protein found in the density 1·063 to 1·21 plasma lipoproteins. Another protein associated with the chylomicrons has been described which is probably identical with a protein found throughout the density spectrum of human plasma lipoproteins. The incorporation of labelled amino acids into these proteins as well as lymph and plasma high density lipoproteins has been studied by the use of dogs with thoracic duct fistulæ and an in-vitro system containing intestinal mucosal cell preparations. Chylomicrons labelled in the protein moiety have also been infused into recipient animals, and attempts were made to determine the fate of the proteins. From a comparison of the specific activities of the chylomicron A protein and the high density lipoproteins obtained in the donor animals, it was concluded that the plasma did not contribute the major portion of this protein found in either the chylomicrons or the high density lipoproteins obtained from thoracic duct lymph. The finding that the intestinal mucosal cells incorporated amino acids into proteins having the same electrophoretic mobility as the chylomicron A and B proteins indicated that the intestine was a source of the proteins of the chylomicrons as well as the protein in the high density lipoprotein fraction. During the disappearance from the plasma of chylomicrons containing labelled proteins there was an immediate appearance of radioactivity in the high density lipoproteins, suggesting a rapid equilibration of the A protein with this fraction. The behaviour of the labelled B protein suggested that it disappeared with the chylomicrons and reappeared in the plasma in a small pool of soluble lipoprotein.

PHYSIOLOGY.

Failure of Manual Artificial Respiration.

P. SAFAR (*J. appl. Physiol.*, January, 1959) discusses the failure of manual respiration and reports that the tidal volumes moved during performance of the back-pressure arm-lift and chest-pressure arm-lift methods in 29 curarized, anæsthetized, apnœic adults were measured with a spirometer through an oro-nasal mask (with and without an artificial oro-pharyngeal airway in place) and through a tracheal tube. With the conventional back-pressure arm-lift method without an artificial airway the average tidal volume was zero, or less than dead space air in 12 of 15 subjects studied. The failure was mainly due to pharyngeal obstruction by the relaxed tongue, occurring when the neck was flexed and the mandible was not supported. An artificial oro-pharyngeal airway only slightly improved the tidal exchange. A modified back-pressure arm-lift method, which consisted of the head being tilted backward, increased the tidal volume and decreased the incidence of obstruction. With the conventional chest-pressure arm-lift method, the tidal volumes likewise depended mainly on the position of the head and neck. A modified chest-pressure arm-lift method, which consisted of maintaining the head tilted backward by elevating the shoulders, was compared in 10 subjects with the modified back-pressure arm-lift method. The tidal volumes were greater and the incidence of upper airway obstruction was lower with the modified chest-pressure arm-lift method. With a tracheal tube in place, tidal volumes of 260 to 840 ml. were moved without signs of airway obstruction. The low values occurred in short and obese patients with reduced lung-thorax compliance.

Continuous Cold Exposure and Nocturnal Body Temperatures.

M. B. KREIDER *et alii* (*J. appl. Physiol.*, January, 1959) report that the effects of continuous cold stress on 24-hour patterns of body temperature were studied in five men. Cold stress consisted in living at 15·6° C. (60° F.) for 14 days wearing only shorts. The cold period was preceded and followed by two weeks at 26·7° C. (80° F.). Activity (minimal) and diet were the same for all periods. One blanket was used at night. Rectal temperature (T_r) and skin temperature (T_s) were measured. T_r during sleep fell more rapidly and to lower values during cold exposure (35·6° C.) than during the control period (36·1° C.). T_s during sleep was slightly lower in the cold than in the control period; also, T_s did not exhibit the gradual drop characteristic of sleep in the control period. Comparison of T_r and T_s between early and later cold days revealed the following differences: (*a*) nocturnal T_r fell to lower levels on the later cold days; (*b*) nocturnal toe temperatures were 15° C. (27° F.) higher on the later cold days. The arch temperatures followed the same pattern as the toes. No significant differences were found in daytime temperatures between early and later cold days. The data suggest that evidence for acclimatization to cold in terms of altered body temperature responses may be fruitfully sought in responses during rewarming, during sleep, or while the subject is being rewarmed during sleep.

Pulmonary Congestion and Vagal Afferent Activity.

L. L. COSTANTIN (*Amer. J. Physiol.*, January, 1959) states that pulmonary venous occlusion was shown to increase the activity of slowly-adapting pulmonary stretch receptors by mechanical alterations within the lung parenchyma. Two types of response were evident, stimulation throughout the respiratory cycle and stimulation only during periods of low lung volume. Pulmonary arterial occlusion caused both significant increases and decreases in vagal fibre activity. Two fibres demonstrated cardiac-triggered impulses superimposed upon a basic respiratory rhythm, an effect dependent upon pulsation of the pulmonary arterial tree. The results of this investigation indicate a twofold responsiveness of the pulmonary stretch receptors, i.e. to the volume of air in the lungs and, to a lesser extent, to the degree of distension of the pulmonary vasculature. The latter effect is suggested as an important factor in explaining the production of a decreased depth of respiration during pulmonary congestion.

Airway Resistance Measurement in Man.

R. G. BARTLETT, JR., *et alii* (*J. appl. Physiol.*, January, 1959) describe a broadly applicable method for the quantitative and continuous measurement of airway resistance in man. It permits the simultaneous measurement of air flow (breath velocity) and alveolar pressure during any breathing pattern. Alveolar pressure is calculated from body plethysmograph pressure (plethysmogram) changes coincident with the compression and expansion of lung air, during expiration and inspiration respectively. The plethysmograph interior is maintained at body temperature and complete H_2O saturation. This avoids the errors in measurement due to plethysmograph pressure changes produced by temperature and humidity changes in the inspired and expired breath and also obviates the necessity of using only a panting type breathing pattern. Data on three normal subjects at near resting and near maximum breathing efforts are presented and discussed. This improved method, permitting airway resistance measurements during any breathing pattern, should find application in diagnosis and assessment of treatment of pulmonary diseases as well as in the investigation of several basic pulmonary function problems.

Mechanical Aspects of the First Breath.

E. AGOSTONI *et alii* (*J. appl. Physiol.*, November, 1958) report a study of the mechanical features of the first breath on mature fœtuses of the guinea-pig, cat and goat. The first inspiration encounters a marked resistance due to the high viscosity of the liquid present in the airways, to the surface tension of the air-liquid interphase, and to the fact that the expansion of the thorax is accomplished only by the inspiratory muscles and is not appreciably facilitated, as in the adult, by the tendency of the thorax to expand owing to elastic forces. Because of these factors the first inspiration may not fulfil its practical purpose and many breaths are necessary before all the liquid is removed and the lung completely aerated. The mechanical features of the lung at birth are similar to those of the adult with regard both to the pressure-volume curves and to hysteresis.

Respiratory Responses to Carbon Dioxide at Different Altitudes.

D. J. REED AND R. H. KELLOGG (*J. appl. Physiol.*, November, 1958) have studied the effect of natural sleep on the breathing of three adult males, normally resident at sea level, at sea level, during a four-week sojourn at 14,250 feet, and after return to sea level. In each case the respiratory minute volume decreased by about two litres per minute during sleep. To investigate the role of altered responsiveness to carbon dioxide in this effect of sleep, graded carbon dioxide mixtures containing sufficient oxygen to preclude hypoxia during the test were administered to the subjects while awake and while asleep. At sea level, sleep shifted the curve relating respiratory minute volume to alveolar carbon dioxide tension (carbon dioxide response curve) to the right by 3 to 5 mm. of mercury, so that higher carbon dioxide tensions were required to stimulate a given level of ventilation. In the tests at high altitude the waking carbon dioxide response curve was 10 to 12 mm. of mercury to the left of its sea level position. During sleep at high altitude the curve shifted to the right from this new position by 3 to 5 mm. of mercury, suggesting that the effects of sleep were superimposed on the respiratory readjustment accompanying high-altitude acclimatization. There was little if any change in shape or slope of the carbon dioxide response curve obtained during natural sleep either at sea level or at high altitude.

Flow of Lymph from the Canine Liver.

H. D. RITCHIE, J. H. GRINDLAY AND J. L. BOLLMAN (*Amer. J. Physiol.*, January, 1959) report that observation of the hilar lymphatics from 100 canine livers seen at operation disclosed two drainage pathways, a main hilar system, draining predominantly the right lobes, and an accessory hilar system, draining mainly the left lobe. In 94% of the animals all of the hilar lymph seemed to pass into one common efferent trunk, which then discharged it into the cisterna chyli. From a study of five dogs in which the gall-bladder was removed and the common bile duct ligated and in which there were fistulæ of both the hilar lymph trunk and the thoracic duct, it was concluded that, normally, about 80% of the lymph leaving the canine liver probably travels by the hilar route and the remaining 20% by the hepatic venous lymph route. The mean flow of hilar lymph from the liver during biliary obstruction in 20 unanæsthetized animals was 0·66 ml. per kilogram of body weight per hour.

Medical Societies.

MEDICAL DEFENCE SOCIETY OF QUEENSLAND.

ANNUAL MEETING.

The fifty-seventh annual meeting of the Medical Defence Society of Queensland was held on Wednesday, April 22, 1959, at B.M.A. House, 88 L'Estrange Terrace, Kelvin Grove, Brisbane, DR. F. W. R. LUKIN in the chair.

Annual Report.

The annual report for the year ended December 31, 1958, was adopted. The report is as follows.

Membership.

The membership of the Society is now 941 as against 882 last year. During the year 94 new members were elected and six returned from overseas. Our losses were as follows: left the State, 29; resignations, 6; deceased, 6.

There are 16 members who have indemnity insurance cover with other approved organizations.

Obituary.

We regret to record the deaths of the following members: Dr. E. Greenham, Dr. R. F. Craig, Dr. G. W. Macartney, Dr. Harold Crawford, Dr. J. J. Luddy and Dr. F. J. Booth.

Office Bearers and Council, 1958.

The following office bearers were elected by the Council: *President,* Dr. F. W. R. Lukin; *Vice-President,* Dr. Athol Quayle; *Honorary Treasurer,* Dr. T. V. Stubbs Brown; *Honorary Secretary,* Dr. D. R. L. Hart; *Councillors for 1958,* Dr. B. N. Adsett, Dr. T. R. Biggs, Dr. H. W. Horn, Dr. N. W. Martin, Dr. Robert Miller, Dr. W. J. Saxton, Dr. J. G. Wagner.

Dr. D. R. L. Hart, Dr. N. W. Martin and Dr. Robert Miller were elected to fill the vacancies caused by the resignations of Professor Neville G. Sutton, Dr. G. W. Macartney and Dr. F. Garrett Scoles.

Medico-Legal.

During the year six cases were submitted to the Society for advice or action, and five were carried over from the previous year. All were dealt with to the satisfaction of the Society and of the members concerned. Of the five cases carried over from last year, writs have been issued in two which the Society is defending. Other matters on which members sought advice were dealt with by the Council or the Secretariat.

General.

Following correspondence with the Medical Defence Union of London and receipt of an undertaking by the Union that it would provide similar cover to that given by the Medical Protection Society and would agree to conduct any litigation through our solicitors or their counsel, it was agreed to recognize the Medical Defence Union as an approved organization for the provision of indemnity cover under Article 21A.

During the year all members of the Society who are insured with organizations other than the Medical Protection Society have been requested to pay their subscriptions in future through the Secretary. It is hoped that all the members concerned will agree to this procedure, which is suggested in their own interests, to ensure that their subscriptions are kept up to date, and which is in accordance with the provisions of Article 21A.

With a view to improving the Society's financial position, Council has resolved that up to 50% of the Society's funds, at present invested in Commonwealth Loan, should be reinvested in semi-government securities bearing higher rates of interest. This policy is being implemented as the various loans mature.

Finance.

It will be shown by the balance sheet that the net surplus for the year ended December 31, 1958, amounted to £570 17s. 6d.

Some items of income and expenditure are as follows:

RECEIPTS:	£	s.	d.
Annual subscriptions, Medical Defence Society of Queensland	538	16	4
Entrance fees	108	3	0
Subscriptions indemnity insurance, Medical Protection Society Ltd., London	6350	6	1
Interest—			
Commonwealth Government inscribed stock	334	3	1
Commonwealth Savings Bank	3	3	9
National Bank of Australasia	63	13	1

EXPENDITURE:	£	s.	d.
Amount remitted to Medical Protection Society	8,051	15	6
Secretarial and clerical assistance	302	0	0
Postages, duty stamps, bank charges, printing and stationery	119	6	8
Audit fee	18	18	0
Legal expenses	29	11	1
Federal income tax for year ended December 31, 1957	38	8	0

The total assets of the Society amount to £12,271 8s., which include the following cash balances:

	£	s.	d.
National Bank of Australasia Ltd.	1471	11	10
Commonwealth Bank of Australia	119	10	4
Petty cash	6	2	11

An amount of £9120 is invested in Commonwealth Government inscribed stock, and £1500 is invested in Brisbane City Council inscribed stock.

Balance Sheet.

The balance sheet and financial statement for the year ended December 31, 1958, was adopted.

Election of Councillors.

The following councillors, who had retired in conformity with the Articles of the Society, were unanimously reelected: Dr. T. V. Stubbs Brown, Dr. W. J. Saxton and Dr. J. G. Wagner.

Election of Auditors.

Messrs. Groom, Sanderson and Company, Chartered Accountants, were reelected auditors for the ensuing year.

Special Correspondence.

LONDON LETTER.

FROM OUR SPECIAL CORRESPONDENT.

Maternity Services.

THE maternity services in Great Britain are divided between the hospitals, the local health authorities and the general practitioners. This tripartite arrangement has been much criticized. In 1956, the Minister of Health appointed a committee under the chairmanship of Lord Cranbrook to review the organization of the maternity services and to make recommendations. Their report, recently published, recommends the retention of the present structure but with improved coordination and cooperation between the three branches and a more uniformly high standard of antenatal care.

Home or Hospital Confinements.—During the past 25 years, in England and Wales, there has been a progressive increase in the proportion of confinements taking place in hospitals or maternity homes, from 39·7% in 1937 to 64·6% in 1957. This trend is more pronounced in other countries—e.g., there is an almost 100% institutional confinement rate in U.S.A., Sweden and Australia. There are many reasons why women prefer to have their babies in hospital; it is thought to be safer, less disruption of home life occurs, the mothers are said to get a complete rest, and there is a widely held opinion that it is cheaper, although it is probably more expensive to public funds. Housing conditions are clearly an important factor. The Royal College of Obstetricians and Gynæcologists, when consulted, considered that confinement in hospital offered maximum safety for mother and baby. However, many witnesses before the committee were concerned with the dangers of infection, and fears were expressed that hospital infection would become more serious in the future. There was general

agreement that hospital provision should be made for all cases in which there were medical or social factors which would make a home confinement undesirable; and the committee has recommended that the hospital maternity service should be expanded to provide for a national average of 70% of all confinements, with a good maternity service for all those women who do not require, for medical or social reasons, to be confined in hospital. A more careful selection of patients should be made for domiciliary confinements and for admission to hospital. Hospital beds would be required for all primigravidæ, for those for whom confinement at home is planned and who require emergency admission, for all patients in whom there is an abnormality or in whom one might be anticipated, and for patients admitted on social grounds. The committee does not believe that it is likely that all women in this country will wish to have their babies in hospital.

Ante-Natal Care.—The importance of regular periodical examinations is stressed, and a high standard of ante-natal care is regarded as essential. The examinations should follow the recognized practice of being monthly to the twenty-eighth week of pregnancy, fortnightly until the thirty-sixth week, and then weekly until confinement. Health education and mothercraft should be available to all expectant mothers. The committee further recommends that ante-natal beds, over and above those needed for confinements, should be provided for some 20% to 25% of confinements. Ante-natal care is at present mainly carried out by the medical officers of the local authorities, who also provide instruction in health education and arrange home helps for expectant mothers. The committee recommends that local authorities should provide premises and facilities, without charge, to general practitioner-obstetricians, who are increasingly replacing medical officers of the local authorities. A minimum qualifying standard for the general practitioner-obstetrician is also recommended.

The success of a maternity service is to be measured by the saving of life, by the improvement in the standard of health of mothers and babies and by the extent to which it can diminish the fears, difficulties and discomforts which have to be faced by every woman who embarks on motherhood. While encouraged by the improvements of the past 20 years, the committee believes that further improvement is possible in the light of present-day medical knowledge and available resources.

Radiation Hazards.

The hazards of ionizing radiation have been widely publicized, and public awareness of the dangers of exposure from such sources as X rays calls for pronouncements from official sources. Without reassurance, the public might become unnecessarily suspicious and the individual patient reluctant to have an X-ray examination. Radiology plays such an important part, not only in diagnosis, but also in treatment, that much individual suffering would follow any curtailment of this service.

The nation-wide survey, at present in progress, of radiological procedures in order to estimate the present level of radiation to which the population is exposed, is the most detailed of its kind ever undertaken in any country. During a selected week, the number and types of X-ray examinations, the number of films used and the apparatus available in all hospitals, chest clinics, dentists' surgeries and other institutions were surveyed. A second census, taken at a different time of the year, was made on a random selection of a quarter of the National Health Service hospitals and chest clinics. At the same time, assessments have been made of the dose received by patients under the varied conditions of different types of radiological examination. A separate investigation is being carried out, including a three months' survey, to estimate the contribution from radiotherapeutic procedures. All this involves a very considerable task of computation. One part of the survey has been completed, i.e., that dealing with mass miniature radiography.

The committee undertaking the survey, under the chairmanship of Lord Adrian, considers it advisable to provide an interim report on the subject without waiting for the completion of the whole of the investigations, as the value of mass radiography is so great that it must not be curtailed without good cause. They point out that mass X-ray examinations in 1957 led to the discovery of nearly 18,000 cases of pulmonary tuberculosis and some 63,000 other abnormalities, which included lung cancer, heart disease and pneumonoconiosis. As a result of this specific survey, the committee thinks it important to state that these examinations, properly conducted, make a negligible contribution to the total radiation to which the population is exposed. A recommendation is made that mass radiography should not be used as a case-finding procedure in children or pregnant women. In pregnant women, the need for routine chest X-ray examinations is recognized, but pelvic X-ray examinations should not be undertaken as a routine procedure.

The committee sees no reason to doubt the conclusions of the Medical Research Council Committee that the major contributions to radiation come from a few types of examination, already known by radiologists as calling for special precautions.

From a preliminary study of the general results of the survey, it is unlikely that the committee will recommend a drastic reassessment of the place of diagnostic radiology in medicine and dentistry.

The Cost of Prescribing.

The gross cost of drugs made available by prescription in the National Health Service has doubled in nine years. If we take into account the fall in the value of money during that period, the real increase is about 45% since 1949-50.

The Hinchcliffe Committee, appointed in 1957 to investigate the factors contributing to the cost of N.H.S. prescriptions, has concluded that "while there is no evidence of widespread and irresponsible extravagance in general practitioners' prescribing, there is scope for economy. The aim should be to keep the Service as economical as possible, compatible with the best available modern treatment, to ensure good value for money and to check waste". In the committee's view, the introduction of a free and comprehensive health service and the discovery and large-scale production of valuable but expensive new drugs are the main factors contributing to the present cost of prescriptions. The tremendous benefits derived from the newer preparations, not only in the relief of suffering and saving of life, but also financially, must not be overlooked. With the aid of drugs, patients can now often be treated at home for conditions formerly treated in hospital.

Concerning the doctors' right to prescribe, the committee has reviewed the methods for the control of the supply of medicines under the Social Security Schemes of Australia, New Zealand and Denmark. They have decided that the doctor must be the sole judge of his patient's requirements for treatment. The medical profession, as a whole, they feel, would oppose any suggestion of direction from above by a committee with the power to decide which drugs are to be freely available and for which diseases they are to be prescribed. A permitted list of free drugs would give rise to the idea that there were two kinds of medical practice and two kinds of medicine—in other words, a second-class service for those who could not pay. There should be no financial barrier between the doctor and his patient.

Among other recommendations are the following. All medical schools should be encouraged to take an interest in economy in prescribing. More students should spend short periods with general practitioners. There is a need for post-graduate instruction of general practitioners in pharmacology and therapeutics. The average practitioner is unable to judge the validity of the makers' claims for the many new drugs now produced. Practitioners should be given more information about the cost and the pros and cons of new drugs by the publication of a journal produced by the appropriate professional bodies. New drugs should be subjected to independent controlled trials and the results published as early as possible.

The Drug Industry.

Much has been said about drug firms and their profits, and a few points may be mentioned that provide food for thought. The drug industry played an important and progressive role in the development of the National Health Service and had to face unusual risks. The sudden discovery of a new form of therapy anywhere in the world could put a product on which a great deal had been spent off the market overnight. The pharmaceutical firms which engage in research have contributed much to therapeutic progress, but the yearly amount spent in this country, viz. £4,000,000, is considered inadequate compared with £7,000,000 in Switzerland and £43,000,000 in the U.S.A.

Poliomyelitis Vaccination.

By the end of February nearly 8,000,000 persons in Great Britain had received at least two injections of poliomyelitis vaccine. For children under 15 years of age, the acceptance rate was 64%. For the most recently eligible group (15 to 26 years) the rate was only 8%. By the end of April this figure showed a sharp rise to 25%, following the announcement of the death from poliomyelitis

of a well-known professional footballer. A personal message from the Minister of Health broadcast at all major league football club matches offering vaccination free to all those under 26 years of age undoubtedly contributed to the dramatic rise in the acceptance rate.

Correspondence.

TETANUS PROPHYLAXIS.[1]

SIR: The appearance in the Journal (February 7, 1959) of two articles and subsequent letters on the subject of tetanus prophylaxis have prompted the writing of this letter. The use of tetanus antitoxin is subject to a number of serious objections which may be listed as follows.

The opening sentence of the special article by the Commonwealth Serum Laboratories' staff states: "At the present time the types of wounds most likely to produce tetanus cannot be determined by clinical methods." This statement is supported by such papers as those of Pratt (1943), Dietrich (1940) and Cole (1951), which emphasize the trivial nature of the wound, if it can be found, in the majority of cases. Moreover, in the examination of children with tetanus (nine of 16 patients admitted to this hospital with tetanus in the last eight years were in the age group 5-13, eight of the nine being males) one may be also perplexed by the multiplicity of trivial wounds, particularly on the feet, and it may be impossible to decide which would is the site of infection. The lists of wounds which are stated by some authors to be likely to give rise to tetanus (e.g., Gissane and Lowbury, quoted by Parish, Laurent and Moynihan, 1957) are so comprehensive as to emphasize the impossibility of deciding on clinical grounds.

Ackland (1959) says: "My own feeling is that it is impossible to differentiate those cases which are so trivial that they can be ignored, and it is, therefore, wise to give protection in every case associated with a breach of the skin surface." It seems obviously impossible to use tetanus antitoxin in this way, for in the majority of these wounds a doctor is not consulted, and also the repeated administration of tetanus antitoxin has certain grave disadvantages. Thus, it has been shown by Sacquepée and Jude (1937) and also by Mahoney and Moloney (1958) that the previous injection of horse serum may result in the very rapid disappearance of tetanus antitoxin, and tetanus has been reported to have occurred apparently due to this phenomenon (Littlewood, Mant and Wright, 1954). Payling Wright (1958) states that once a person has been injected with horse serum proteins no reliance could be placed upon his protection by A.T.S. should he subsequently be exposed to the risk of tetanus. Moreover, the immunity conferred even in those not previously injected, if it be judged by the presence of circulating antitoxin in the blood, is often very short. Thus, of 98 patients not previously injected with A.T.S., tested 10-12 days after a prophylactic dose of 1500 units A.T.S., 41 had no circulating antitoxin (Mahoney and Moloney, 1958).

Further, it would appear that reactions are more common in those who have previously been injected with horse serum. Lyall and Murdick (1938) reported that 13·5% (110) of 815 accident patients had had previous A.T.S., and that in 23·6% of these a generalized reaction occurred to another A.T.S. injection, compared with 8·8% in those who had not had such prior injection. Mahoney and Moloney found that 71% of patients with a systemic reaction to A.T.S. had had previous horse serum.

The dangers and sequelæ of the use of horse serum are very difficult to estimate, and depend upon many factors, such as the refinement of antiserum, previous injections, dosage, route used, circumstances in which A.T.S. is given, knowledge of attending doctor regarding the wide variety of reactions, and it seems likely that they are often unrecognized. Miller and Stanton (1954) state: "It must be admitted that, in the heat of the emotional battle provoked by propaganda for and against prophylactic inoculation, there has been a tendency on the part of the medical profession to turn a blind eye to unfortunate individual complications of procedures which have the indisputable sanction of social value." The complications of horse serum injection range from minor local reactions through reactions of gradually increasing severity such as generalized urticaria, arthralgia, signs and symptoms of heart, lung and kidney involvement to neurological complications, some of which are of considerable danger to the patient, with cases of radiculitis, brachial plexus neuritis, polyneuritis, Guillain-Barré syndrome, myelitis and cerebral and meningeal reactions (Miller and Stanton, 1954; Woolling and Rushton, 1950).

The fact that about 70% of reports in the literature of neurological complications following serum injection are from French sources very probably merely indicates a greater awareness of these complications in France. The complications and failure of therapy such as serum and vaccine injections and blood transfusions are very rarely recorded in the literature even when recognized, with the result that the true risk of the therapy can only be guessed at, often indirectly (e.g., examination of the case reports of the patients who were treated by the artificial kidney at Sydney Hospital (Edwards and Whyte, 1959) reveals some dangers of blood transfusion).

The danger of death from immediate anaphylactic reaction or protein shock is difficult to assess; figures have been quoted as low as 1 in 1250 (Kojis, 1942). Moynihan (1956) had two cases of non-fatal anaphylaxis in 7580 cases, Laurent and Parish (1952) quote "various authors" to estimate the risk of death at 1 in 50,000 to 1 in 200,000 but do not state the source of information; the latter believe that the incidence may not have been lowered by modern processing. The risk of allergic reaction is increased by previous administration of horse serum, but there seems little doubt that fatal protein shock can occur in persons not previously injected with foreign serum, particularly asthmatics (Vance and Strassman, 1942). In the report of the British Ministry of Health (1954) the following statement appears: "The administration of anti-tetanus serum is particularly liable to be associated with severe serum reactions and in the five years 1950-1954 no fewer than nine deaths were certified as occurring from anaphylaxis or allergy following its administration." The number of doses of A.T.S. given is unfortunately not known, according to a letter received from the British Ministry of Health. Skin testing would appear to be unable to predict accurately the occurrence of anaphylaxis (Mahoney and Moloney, 1958; Laurent and Parish, 1952), and it also seems unlikely that desensitization can be achieved (Moynihan, 1956).

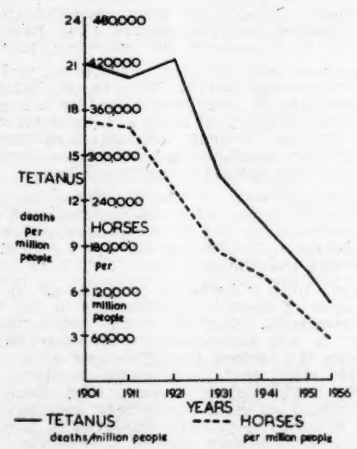
Press (1948) also quotes a number of references which testify to what is generally known—that practically any study of the illness reveals many cases in which tetanus antitoxin failed to prevent tetanus; and this author gives an average of figures quoted in the literature showing that 33·4% of cases which had developed tetanus had received prophylactic antiserum (the average in non-military cases was 6·8%). Thus is it seen that antiserum is by no means efficacious in the prevention of tetanus in humans; also, in these cases the patient not only has the risk of contracting tetanus, but has the added risk of the complications of therapy. It may be said that A.T.S. is not given in the correct manner, that the patient should continue to have injections of A.T.S. until the danger of getting tetanus is no longer present, whenever that may be, or that the dose should have been greater. Bruce (1920) found that multiple prophylactic injections did not in fact favourably influence mortality rate, and it is interesting to think that the drop in the incidence of tetanus in World War I, which is said to constitute major evidence in support of prophylactic A.T.S. being of value, occurred at a time when one injection of 500 units was given.

The question then arises: What is the doctor to do when confronted by a patient with a wound? It seems obvious that A.T.S. could not be given more than once. The usual answer is to give prophylactic A.T.S. "if indicated" and then later actively immunize him. As the risk of any treatment should not increase the hazard to the patient, the point to be decided is: are the risks of giving tetanus antiserum for one particular wound less than the risk of the patient getting tetanus? (as stated by Dr. Taylor in his letter to the Journal). This question appears almost impossible to answer, as will be shown. According to the figures obtained from the N.S.W. Statistical Register for the years 1952-1955, deaths from tetanus in N.S.W. in the years 1952, 1953, 1954, 1955 were 11, 27, 18 and 19 respectively, averaging 19 per year and giving a rate of 1/180,000 based on a mean population of 3,450,000. Thus the chance of developing tetanus from a particular wound in this period would be $\frac{1}{180{,}000 \times x}$ where x = the number of wounds suffered per person per year which could have given rise to tetanus, and where there is an equal risk of sustaining tetanus from any one wound. This unknown figure x is obviously of very considerable

[1] A full list of references was supplied but has been omitted for reasons of space.

importance, but I am unaware of information on this point; it is obvious that it would vary widely from age group to age group etc., but children particularly are constantly suffering wounds which may cause tetanus, and any week-end gardener is at great risk. Thus if one were to take $x=10$, surely in children a value much below the real figure, then the risk of dying from tetanus in a particular wound would be $\frac{1}{1{\cdot}8\times10^6}$ which seems considerably less than the risk from the various complications of A.T.S. One should also remember that A.T.S. by no means ensures that the risk of $\frac{1}{1{\cdot}8\times10^6}$ is reduced to nil, but does in fact often add the risk of complications of treatment. Thus it seems reasonable to ask: "Should A.T.S. be given at all?"; and on the basis of these calculations the answer is "no".

It may be argued that the prophylactic use of tetanus antitoxin in certain cases, particularly those wounds which are "likely" to develop tetanus, has lowered the incidence and the mortality, and so the risk of tetanus would be much greater than I have stated if A.T.S. were not used. In answering this, one can only reemphasize that tetanus is a disease occurring very largely in relation to trivial wounds in civilian practice, and that it is impossible to predict which wound will give rise to tetanus, as is shown by examination of many published cases. Should it be thought that this state of affairs has been brought about by the use of prophylactic A.T.S., one may say that this occurrence in trivial wounds was also a feature of the cases reported by Cooper (1917), when no prophylactic A.T.S. was used in the community. Furthermore, an examination of the tetanus mortality figures in N.S.W. does not support this view. When graphed in ten-year means, it is seen that there has been a decline since the early years of the third decade of this century, and that this decline closely parallels the fall in the horse population of the State (expressed in terms of horses per million people—see graph). It is interesting to consider the possible meaning of this graph; it would be as logical to assume a causal relationship as it would be to assume the same relationship between the use of prophylactic tetanus antiserum and declining mortality.



Moreover, good evidence that tetanus antitoxin does in fact prevent tetanus is difficult to find in the literature, and it would be interesting to know what is supposed to constitute evidence to this effect by the proponents of the use of prophylactic A.T.S. The value of therapeutic antiserum seems even more questionable, if possible, than that of prophylactic A.T.S.; Bruce (1920) seriously questions its value, Golla (1917) was of the opinion that it did not lower the mortality rate, Huntington, Thompson and Gordon (1938) could find no evidence that it was of value, nor could Johnstone (1958) or Pratt (1943). It is interesting to reflect that an editorial of *The Lancet* in 1917 stated: "To Von Behring toxin and antitoxin may well have appeared as chemical antidotes capable of neutralizing one another, although Ehrlich, at all events, never considered them to be simple substances of strong affinity, like caustic soda and hydrochloric acid."

The medico-legal question is always raised, particularly in the case of tetanus and the giving of A.T.S., although why it should be more of a crime not to give A.T.S. than not to perform another "recognized" procedure, wound débridement, it is difficult to understand. It would seem that if the figures quoted are correct, then a doctor who gives tetanus antitoxin should rather be sued for exposing the patient to unnecessary risk should serious complications of therapy arise. In fact large sums of money have been paid by insurance companies to patients suffering from the complications of serum therapy (Bennett, 1939).

German opinion on this point is of interest, and at the 73rd Annual Meeting of the German Society of Surgery a number of resolutions in regard to the control of tetanus were carried, several of which may be quoted:

(2) (c) There are no generally valid indications for serum prophylaxis.

(4) Tetanus can only be prevented by means of active immunization of the whole nation.

(10) *Further, it should not be expected of the doctor that he should alone carry the responsibility of preventing tetanus after each fresh wound. On principle, we do not agree that the omission of the usual but ineffective preventive measures in any isolated case, is a defect in medical care, or grounds for litigation.*

(This paragraph in italics in the original German).

Is it reasonable to assume that the patient, or the patient's parents, have some responsibility in this matter to see that active immunization is performed? Should it be in part the responsibility of the medical profession to educate the public, or the legislature?

There seems little doubt that the only logical and effective method of prevention of tetanus is by active immunization, and there is good evidence in the literature to support this (e.g., Boyd, 1946; Boyd and McLennan, 1942, reporting on British war experiences). Papers also indicate that reasonably high levels of circulating antitoxin are present for some time afterwards (e.g., Moss, Waters and Brower, 1955), although whether these levels reflect the true defence mechanism of the organism is another matter.

Whether mass immunization is justified is difficult to decide in view of the steadily falling incidence of the disease; reactions to tetanus toxoid have been negligible (Long and Sartwell); but what data are there as to how many serious reactions will occur in the future with the repeated (say five-yearly) administration of toxoid?

These matters are somewhat contentious, and opinion as to what constitutes evidence may vary; the views of others on this difficult but ever-present problem would certainly be of great interest.

Is it possible that A.T.S., like typhoid vaccine, has been used for so many years with no real proof of its value? Professor W. Bulloch in 1917 is quoted as describing tetanus as a disease in the clinical knowledge of which there has been no advance since the days of Hippocrates, and he went on to marvel that twenty years after the introduction of antitoxin its value to the patient should still be under discussion. Should we marvel even more today, 60 years after?

Yours, etc.,

The Royal Newcastle Hospital. W. F. HUNTER.
Newcastle, N.S.W.
June 1, 1959.

SOME OBSERVATIONS ON INGUINAL HERNIA IN THE ADULT.

SIR: In Mr. Thomas F. Rose's article on inguinal hernia in the adult (MED. J. AUST., June 6, 1959), the work of Hoguet and Coley (1918) is quoted, with a recurrence rate of only 0·38% in the repair of inguinal hernias by Bassini's method in 3725 cases. These extraordinarily low figures of recurrence, in comparison with modern series, led me to a careful study of Hoguet and Coley's original article, which is of considerable interest. However, the various tables of figures are extremely difficult to correlate; this tends to make the article confusing. It would appear possible that the figures quoted for the series of 3725 cases applied only to patients operated on at the Hospital for Ruptured and Crippled, where adult males were admitted only in the year immediately preceding the report.

Later in the same report, an abstract of cases of inguinal hernia observed at the Hospital for Ruptured and Crippled, numbering 4522, is given; of these only 95 were males over the age of 15, 871 were females, of which 313 were over the age of 15. Still further in the article 2499 cases operated on outside the Hospital for Ruptured and Crippled are mentioned, the majority of these (1855) being male, and the preponderance of these males being over 20 years of age. From the figures given it is not possible to tell exactly how many were adult males, neither are figures for recurrences apparently included in this series.

The criteria of establishing recurrence are not mentioned; although the authors state that "a large number" of patients were observed, the remainder were followed up postally, a method which Mr. Rose deprecates. In the series of 4522 previously mentioned, although again it is not made completely clear, it would appear that only 2506 could be followed up at all.

Without detracting from the work of Hoguet and Coley, it seems hardly fair to quote their remarkably low recurrence rates in favour of Bassini's operation. Few surgeons today would recommend any sort of inguinal hernia repair in children under the age of 15.

It is relevant to quote more recent series of figures. H. C. Edwards[1] states that no less than 12% of the inguinal hernias operated on in the United Kingdom may be expected to recur. He recommended discontinuing Bassini's operation altogether. C. MacLeod,[2] in a smaller personal series, showed a recurrence rate of 15% for simple herniotomy in young adult males, and a 17% recurrence rate for the lattice darn method of operative repair in older men.

It was reassuring to see that Mr. Rose condemns the practice of bilateral operation in children who present with unilateral inguinal hernia. Those who practise this admit that less than 20% of the patients operated upon show a sac on the contralateral side. It is difficult to understand the grounds on which such a practice can be justified; in my opinion Mr. Rose's condemnation was both timely and necessary. Many surgeons would disagree with the view that bilateral hernias can be repaired at the same time; the practice of any form of simultaneous bilateral herniopiasty is deprecated by J. Taylor,[3] though no objection is raised to simultaneous bilateral herniotomy in the young, where two hernias are clinically present.

The method of inguinal hernia repair is a vexed question, because the results, even in the best hands, appear so indifferent. Each method has its disadvantages. However, the basic concept in Bassini's repair would appear to be mistaken—i.e., the provision of a rigid posterior wall to the inguinal canal by attaching the muscular conjoined tendon to Poupart's ligament. Many authors stress the importance of maintaining the normal anatomy as far as possible with the minimum of distortion, so that the normal protective muscular action of the inguinal canal is maintained, and particularly that of the internal ring. In my opinion, any procedure which provides rigid support to the posterior wall of the canal, either by fixation of the conjoined tendon or by prosthesis, is liable to interfere, often grossly, with this muscular action. Suture of the conjoined tendon as in Bassini's operation must impair the normal action of the internal ring. But it is agreed that some form of reinforcement to the posterior wall is required in adults, particularly males, and in direct hernias this is a *sine qua non*.

Gallie's operation and the various forms of lattice repairs are in the main fibrosis producers, with the aim of providing a rigid, fibrotic posterior wall. It is doubtful whether strips of detached fascia lata remain viable; certainly, in the small number of fascia lata repairs which I have seen operated upon for recurrence, there has been no sign of living fascia lata, only dense fibrosis.

I would like to make a plea for consideration of a modified Bloodgood's operation, involving strengthening of the posterior wall of the inguinal canal by a semicircular rectus sheath flap, hinged below, turned down and attached with no tension from the region of the pubic tubercle, to Poupart's ligament as far laterally as is necessary. If this flap is properly cut, there is no tension on it, it remains alive, having a broad base; aponeurosis is joined to similar tissue, so firm union can be expected. There is minimal interference with the normal anatomy of the inguinal canal itself, but the medial aspect of the internal ring is greatly strengthened.

There are, of course, objections to this operation, as to all inguinal hernia repairs. Occasionally the tissues making up the flap are so attenuated that the repair is not feasible. In experience of the operation over 13 years I have found this to be unusual. A Spigelian hernia may occur; in one of my patients this has happened, but this patient has no discomfort from the diffuse bulge of the hernia, which appears clinically to consist of extraperitoneal fat.

Mr. Rose calls attention to the possibility of osteitis pubis occurring as the result of inserting sutures into the pubic periosteum, which is an essential step in the rectus sheath flap operation. This is probably a theoretical danger; I have not known it occur in a personal series of nearly 200 operations (not all followed for many years personally, nor until death), neither have I heard of it from surgeons who do the operation. In Lothiessen's repair for femoral hernia, sutures are placed in Astley Cooper's ligament, yet osteitis pubis is not mentioned as a complication of this operation.

Finally, to revert to Mr. H. C. Edwards's excellent review of inguinal hernia surgery, I cannot too strongly emphasize my agreement with him that hernia surgery should never be regarded as minor surgery. If all forms of operation for hernia are regarded as major procedures, to be done with the maximum of care for hæmostasis and asepsis, perhaps our present poor results for this type of operation may show some improvement.

Yours, etc.,

J. D. SIDEY.

Verco Building,
178 North Terrace,
Adelaide.

June 19, 1959.

[1] *Brit. J. Surg.*, 1943, 31: 172.
[2] *Lancet*, 1955, 2: 106.
[3] "British Surgical Practice", 1948, 4: 438.

MEDICAL TECHNOLOGY CONVENTION.

SIR: I refer to a number of letters appearing in your *Journal* under the title of "Medical Technology Convention", written by Dr. Douglas and others, concerning the Australasian Institute of Medical Laboratory Technology.

It appears to our Federal Council that certain misconceptions as to the nature and functions of the Institute may have been conveyed to your readers. Therefore I have been directed to bring before your notice, for the information of your readers, the following information.

1. The Institute was formally constituted and registered under the *Companies Act* of New South Wales in 1936. Prior to this date it had functioned for many years as a branch of the Institute of Medical Laboratory Technology (England). At the present time we have Australia-wide membership, with branches in all States excepting Tasmania and the Australian Capital Territory.

2. The principal aim of our Institute is to promote, advance and develop the scientific knowledge of our profession. The methods by which we endeavour to carry out our aims are those in general use by the British Medical Association and the Colleges.

3. The name of our Institute was chosen in conformity with the names of similar organizations in the other Commonwealth countries. Our use of the words "medical" and "technology" is not inconsistent with their definitions as given by both the Oxford and Webster's dictionaries. Your readers will note that our name includes the word "laboratory". We are well aware that there are many medical technologies, and accordingly membership of our Institute is confined to persons employed in human medical laboratories and veterinary medical laboratories.

4. Medical laboratory technologists employed in diagnostic laboratories and who are members of our Institute are bound by a written code of ethics to work under the direction of a legally qualified medical practitioner. When the shortage of pathologists is overcome, we shall insist that the medical practitioner in question shall be a registered specialist pathologist.

5. We condemn the use of the word "pathologist" when used to describe one of our members. In actual fact it is the lay public who are the greatest offenders in this regard. However, the misuse of the word is aided and abetted by secretaries of hospital boards, who advertise for a "pathologist" when it is obvious that they mean "medical laboratory technologist". Not infrequently one hears general practitioners also loosely applying the name to our members.

6. In order to dispel the impression that our diploma was designed by our Institute alone, we draw your attention to

the fact that the course was designed, and is now governed, by the various State Examining Councils (with the exception of New South Wales). The Councils consist of representatives from the following bodies: The College of Pathologists of Australia, the University's Faculty of Medicine, the State Government Department of Education, and our Institute. It is clear that at least the majority of the members of these councils are persons experienced in education and are mindful of the educational requirements of our profession. These Councils, although appointed under our constitution, are completely independent of the Institute and are in no way controlled by it.

7. Dr. Douglas (MED. J. AUST., May 16) has drawn heavily on the printed matter of the Examining Council in Medical Technology (N.S.W.). As this Examining Council is constituted by the New South Wales Hospitals Commission, the opinions expressed by it are not necessarily the opinions of our Institute. In all fairness we wish to record that the standard of its diploma course is at least equivalent to the course conducted by us.

8. We are at a loss to understand Dr. Douglas's reference (MED. J. AUST., May 16) to a modern Tower of Babel. We were also under the impression that our motives were quite clear.

My Council is well aware that the great majority of the specialist pathologists of Australia are in possession of the above information and are actively engaged in assisting us to further our aims. However, we feel that the recent letters in your Journal may have given your readers a false impression of our activities, and we hope that the above information will place matters in their proper perspective.

Yours, etc.

J. R. SAAL,
Federal Secretary,
Federal Executive Council,
The Australasian Institute of Medical Laboratory Technology.

23 Orient Road,
Yeronga,
Queensland.
June 22, 1959.

AUSTRALIAN AND NEW ZEALAND ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE.

SIR: I should be grateful if I might use your columns to draw the attention of members of the medical profession to the forthcoming 34th Congress of the Australian and New Zealand Association for the Advancement of Science, which is to be held in Perth from August 24 to 28, 1959.

Items of medical interest in the programme include a symposium to celebrate the 100th anniversary of Darwin's "Origin of Species" on Tuesday, August 25, and symposia later in the week on "Medical Education", "Staphyloccocal Infections within Hospitals", "Hospital Design", "Public Health", "Hæmatology", and "Electrolyte Metabolism in Man", as well as varied papers on microbiology, physiology, biochemistry and nutrition.

In addition, the Royal Microscopical Society will be holding an illustrated exhibition.

Yours, etc.

N. F. STANLEY,
Vice-President, Section I—Microbiology, Epidemiology and Experimental Medicine.

Department of Microbiology,
University of Western Australia,
School of Medicine,
Victoria Square,
Perth.
June 29, 1959.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Annual Subscription Course.

THE Post-Graduate Committee in Medicine in the University of Sydney has announced the following lectures in the annual subscription course:

Professor Edward Hon, Assistant Professor of Obstetrics and Gynæcology at Yale University School of Medicine, and visiting Professor in Obstetrics at the University of Sydney, will give the following lecture on Thursday, August 13, at 8.15 p.m., in the Stawell Hall, 145 Macquarie Street, Sydney: "Résumé of Factors Affecting the Fœtal Heart Rate and the Use of the Technique in Related Problems of Cerebral Palsy."

Professor Leo Samuels, Professor and Head of the Department of Biological Chemistry, University of Utah College of Medicine, will speak on "Extra-Adrenal Factors Affecting Cortisol Metabolism in the Human" on Monday, July 20, at 7.30 p.m., in the Main Lecture Theatre, School of Public Health and Tropical Medicine, University of Sydney.

Dr. Robert M. Kark, Professor of Medicine, University of Illinois College of Medicine, Chicago, and Pfizer Lecturer for 1959, will give the following lectures: Monday, July 27, at 8.15 p.m., at The Royal Newcastle Hospital—"Renal Biopsy"; Tuesday, July 28, at 1.45 p.m., in the Students' Lecture Hall, St. Vincent's Hospital, Sydney—"Clinical Features, Pathology and Therapy of Hæmochromatosis"; Tuesday, July 28, at 8.15 p.m., in the Stawell Hall, 145 Macquarie Street, Sydney—"The Management of the Patient with Acute Virus Hepatitis"; Wednesday, July 29, at 2 p.m., in the Maitland Lecture Theatre, Sydney Hospital—"Chronic Liver Disease"; Thursday, July 30, at 2.15 p.m., in the Students' Lecture Hall, The Royal North Shore Hospital of Sydney—"The Nephrotic Syndrome in Adults"; Friday, July 31, at 1.15 p.m., in the Scot Skirving Lecture Theatre, Royal Prince Alfred Hospital, Sydney—"Renal Biopsy".

Professor R. R. H. Lovell, Professor of Medicine, University of Melbourne, and Pfizer Guest Professor to the Royal North Shore Hospital of Sydney, will speak on "The Tenth Anniversary of Cortisone" on Wednesday, August 26, at 8.15 p.m., in the Stawell Hall, 145 Macquarie Street, Sydney.

MELBOURNE MEDICAL POST-GRADUATE COMMITTEE.

PROGRAMME FOR AUGUST, 1959.

Professor Robert Kark.

FROM August 2 to 7, Dr. Robert Kark, Professor of Medicine, University of Illinois, Chicago, will visit Melbourne as the Pfizer Lecturer for 1959. He will give the following lectures, to which all members of the profession are invited without fee:

Medical Society Hall, at 8.15 p.m.:- Monday, August 3, "Management of the Patient with Acute (Virus A) Hepatitis"; Thursday, August 6, "The Nephrotic Syndrome in Adults: A Common Disorder with many Causes".

Royal Melbourne Hospital at 1 p.m. on Friday, August 7, "Histological and Clinical Evolution of Lupus Nephritis" (to the Resident Medical Officers' Club).

Professor Kark will visit the following hospitals: Monday, August 3, morning—St. Vincent's Hospital; Tuesday, August 4, morning, Prince Henry's Hospital; Thursday, August 6, Alfred Hospital; Friday, August 7, Royal Melbourne Hospital (9.30 a.m., Clinical Research Unit ward round; 10.30 a.m., professorial ward round).

Lecture by Professor R. P. Jepson.

Professor R. P. Jepson, Professor of Surgery in the University of Adelaide, will give a lecture on Thursday, August 13, at 8.15 p.m., at St. Vincent's Hospital, on "Carcinoma of the Thyroid". All members of the medical profession are invited to be present without fee. Supper will be served after the lecture, and the Committee requires notification, by August 7, of intention to be present. This lecture has been arranged by the Melbourne Medical Post-Graduate Committee, in collaboration with the Anti-Cancer Council of Victoria.

Country Courses.

Bendigo.—On Friday, August 7, at 8 p.m., at the Bendigo Base Hospital, Mr. G. S. Gunter will speak on "Management of Burns". The local secretary for this course is Dr. M. Clark, 98 Mitchell Street, Bendigo.

Yallourn.—At the LaTrobe Valley Community Hospital, on Saturday, August 8, the following course will be given: 2.30 p.m., "Infertility", Dr. N. Forrest; 4.15 p.m., "Antenatal Care, with Special Reference to Anæmia, Diabetes and

Hypertension, Dr. E. V. MacKay; 7.30 p.m., "Stress Incontinence", Dr. R. Zacharin; 9 p.m., quiz session, with Dr. N. Forrest, Dr. E. V. MacKay and Dr. R. Zacharin forming a panel. The local secretary is Dr. J. E. Joseph, 237 Prince's Highway, Morwell.

Ballarat.—On Thursday, August 27, at 8 p.m. at Craig's Hotel, Ballarat, Dr. S. Williams will speak on "Recent Trends in Antibiotic Therapy". The local secretary is Dr. N. Pescott, 626 Sturt Street, Ballarat.

Fees.— Attendance at the courses at Bendigo, Yallourn and Ballarat is by fee of 15s. per lecture, or by annual subscription to the Committee.

Flinders Naval Depot.

At Flinders Naval Depot on Wednesday, August 12, at 2.30 p.m., Dr. Robert Kelly will lecture on "Common Skin Diseases". This lecture is being given by arrangement with the Royal Australian Navy.

Course in Psychiatry.

The course conducted by the Australasian Association of Psychiatrists at the Royal Melbourne Hospital will continue on Thursdays, at 8.15 p.m., as follows: July 23, Forensic Psychiatry: "The Treatment of the Sexual Offender", Mr. H. Whitaker. Judge Mulvany will contribute to the discussion. July 30, Neurosurgery: "Disturbances of Consciousness and Behaviour of Traumatic Origin", Mr. R. S. Hooper. August 6, Forensic Psychiatry: "Workers' Compensation", Dr. G. Springthorpe. Mr. C. W. Harris, barrister at law, will contribute to the discussion. August 13, Pharmacological Psychiatry: "Drug Therapy in Psychiatry, The Controlled Experiment", Dr. D. Somerville. August 20, Pharmacological Psychiatry: "The Mode of Action of Drugs Used in Psychiatry", Professor F. H. Shaw. August 27, "Uses and Abuses of Ancillary Disciplines", Dr. J. F. Williams.

Dr. G. Springthorpe will be Course Controller on July 23 and August 6, and the chairmen will be Dr. E. Cunningnam Dax on July 30, Dr. A. Stoller on August 13 and 20 and Dr. A. Sinclair on August 27.

REFRESHER COURSE IN PÆDIATRICS.

The Royal Children's Hospital Staff will conduct a pædiatrics refresher course from Monday, August 31, to Friday, September 4, from 9.30 a.m. till late afternoon. The programme is as follows:

Monday, August 31: (i) Symposium on Asthma: "Infection", Dr. T. G. Maddison; "Allergy", Dr. E. K. Turner; "Emotional Aspects", Dr. H. J. Sinn; "Therapy", Dr. D. Galbraith. (ii) Failure to Thrive: "Clinical Aspects", Dr. H. N. B. Wettenhall; "Laboratory Aspects", Dr. J. W. Perry. (iii) Afternoon clinical meeting, case presentations by members of the senior medical staff.

Tuesday, September 1: (i) Symposium on Abdominal Pain: "Surgical Aspects", Mr. R. Howard; "Medical Aspects", Dr. M. Blanch; "Psychiatric Aspects", Dr. W. Rickards. (ii) Orthopædic quiz session: panel, Mr. J. B. Colquhoun and Mr. E. E. Price. (iii) Symposium on Deafness: members of the Hearing Clinic.

Wednesday, September 2: (i) "Prematurity", Dr. Kate Campbell. (ii) "Early Recognition of Surgical Emergencies in the Newborn", Mr. F. D. Stephens. (iii) "Birth Injury", Mr. R. S. Hooper. (iv) Quiz session: "Newborn Problems", panel, Dr. Campbell, Mr. F. D. Stephens, Mr. R. S. Hooper and Dr. J. H. Colebatch. (v) Cardiac demonstration, "Systolic Murmurs". (vi) Cardiac quiz session: panel, Dr. M. L. Powell, Dr. A. W. Venables, Dr. H. Hiller, Mr. N. A. Myers and Mr. P. G. Jones.

Thursday, September 3: (i) "Factors in Adjustment at School", Mr. John Hall (Education Department, Psychology Branch). (ii) "Pædiatric Social Services in Victoria", Dr. Elizabeth Wilmot. (iii) "Medical Problems of Adolescence", Dr. A. M. Hutson. (iv) "Pædiatric Gynæcology", Dr. Kelvin Churches. (v) "Immediate Treatment of Burns", Mr. A. M. Clarke. (vi) Demonstration of dermatological problems, Dr. R. Kelly.

Friday, September 4: (i) "Vascular Lesions of the Skin", Mr. A. R. Wakefield. (ii) "Torticollis and Cranial Asymmetry", Mr. P. G. Jones. (iii) "Common Lower Bowel Problems", Mr. N. A. Myers. (iv) "Long-term Management of Fibrocystic Disease", Dr. C. Anderson. (v) Afternoon clinical meeting, case presentations by members of the Senior Medical Staff.

A fee of £2 2s. will be payable for this course. This will also cover lunch and morning and afternoon teas. It is requested that an enrolment form, obtainable from the Melbourne Medical Post-Graduate Committee, be completed and returned to them by August 10. Further details are obtainable from the Committee, or from the Dean of the Clinical School, Royal Children's Hospital, Pelham Street, Carlton.

RECORDED LECTURE.

The following has been added to the Committee's library of recorded lectures on microgroove disks, and may be borrowed on request: "Clinical Problems of Digitalis Therapy", by Dr. A. Rae Gilchrist, of Edinburgh. (Two ten-inch disks; 15 slides, 2 in. by 2 in.).

FURTHER REFRESHER COURSES FOR GENERAL PRACTITIONERS.

A gynæcology and obstetrics refresher course will be held at the Royal Women's Hospital, full-time, for two weeks commencing on September 7. Limited residential accommodation is available at the hospital.

A refresher course in medicine and surgery will be conducted at the Royal Melbourne Hospital, full-time, during the week commencing September 21.

ENROLMENTS.

Enrolments for all metropolitan courses described above should be made with the Melbourne Medical Post-Graduate Committee, 394 Albert Street, East Melbourne. Telephone FB 2547.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

LEPROSY IN NEW SOUTH WALES.[1]

[From the *Australasian Medical Gazette*, November, 1896.]

THE report for 1895 of the N.S.W. Board of Health upon the administration of the Leprosy Act was laid on the table of the Legislative Assembly in Sydney on November 5th by the Premier. At the beginning of 1895 40 persons remained under detention at the lazaret. During the year 10 persons were reported to the Board as being suspected lepers, and three of these were eventually admitted to the lazaret. The number of deaths during the year was 5, and one patient was discharged. This patient was admitted in 1888, when only 14 years of age, and from the time he fell under observation his symptoms gradually receded, until, so says the report, as far back as two or three years ago little remained but some deformities. These were evidence, not of active disease, but of disease which had existed, and which had caused the mutilations during the bygone time of its activity. In view of the apparent recovery of the patient, his relatives had for some time made repeated applications for his release, but the Board felt themselves unable to grant it until they had satisfied themselves, both by lapse of time and repeated examination, that no danger to the public health would result. This conclusion being at last, in their opinion, warranted, and the relatives of the patient having shown to the satisfaction of the Board that they were able and would provide suitably for his care and keep, the Board authorized his discharge. The number remaining in the lazaret at the end of the year was, therefore, 37. Of these, 16 were whites—four of them being females—while the remaining 21 were members of various coloured races. The total number of patients admitted since 1883 when the first patients were received is 58.

[1] From the original in the Mitchell Library, Sydney.

Royal Australasian College of Surgeons.

VICTORIAN STATE COMMITTEE.

Course in Surgery for F.R.A.C.S.

THE Victorian State Committee of the Royal Australasian College of Surgeons will conduct a course in surgery for the F.R.A.C.S., to commence in Melbourne on Monday, August 3, 1959, and continue full-time until

October 9. Formal instruction commences at 2 p.m., and comprises a comprehensive series of over 50 lectures from surgeons of all the clinical schools and specialties. These are given at the Royal Melbourne Hospital, the Alfred Hospital, St. Vincent's Hospital, Prince Henry's Hospital and the Royal Children's Hospital on four afternoons each week, and are followed by a demonstration of clinical cases at the same hospital from 4.15 to 5.30 p.m. Special demonstrations in radiology and pathology have also been arranged at each of these hospitals. On each Wednesday afternoon of the course, special demonstrations have been arranged at the Austin Hospital, the Eye and Ear Hospital, Frankston Orthopædic Hospital, Heidelberg Repatriation Hospital, the Royal Women's Hospital and the Queen Victoria Hospital, and at the Peter MacCallum Clinic, by the courtesy of the authorities at each of these institutions.

This course is designed to prepare candidates for the final examination for F.R.A.C.S. in October. The fee for the full course is 20 guineas (clinical demonstrations only, 10 guineas), payable to the Honorary Secretary, Victorian State Committee, Royal Australasian College of Surgeons, Spring Street, Melbourne. Entries will be accepted up to July 31, 1959.

Notes and News.

Australian Society of Anæsthetists' Prize for Anæsthetic Registrars.

The Australian Society of Anæsthetists awards an annual prize of £25 for the best original paper submitted by an Australian anæsthetist holding the grading of senior registrar or under. It is not necessary that he or she be a member of the Society. The subject of the paper is optional, but must be related to anæsthesia. It is desirable that papers submitted show evidence of personal work; but papers consisting of surveys of the literature are eligible for consideration. The paper must not have been previously read at any meeting or published in any journal. The winner of the prize will be invited to read his paper at the annual general meeting of the Australian Society of Anæsthetists. The Society will give every assistance in obtaining publication of the paper in a recognized medical journal. Papers for adjudication should reach the Honorary Secretary, Dr. Patricia Wilson, 132 Grey Street, East Melbourne, Victoria, not later than December 1, 1959.

Pfizer Travelling Fellowship in Clinical Medicine (Australia).

On the recommendation of the Council of The Royal Australasian College of Physicians, the Pfizer Travelling Fellowship in Clinical Medicine (Australia) for 1960 has been awarded to Dr. S. J. M. Goulston, of the Royal Prince Alfred Hospital, Sydney.

The Arthur Wilson Memorial Lecture.

The Regional Council in Australia of the Royal College of Obstetricians and Gynæcologists announces that the sixth Arthur Wilson Memorial Lecture will be held on Friday, August 21, 1959, at 8.15 p.m., at the College House, 8 Latrobe Street, Melbourne. The lecturer is Professor Gordon King, Professor of Obstetrics and Gynæcology at the University of Western Australia, and his subject will be "The Changing Art of Obstetrics". All members of the medical profession are invited to the lecture and afterwards to supper.

International Conferences on Obstetrics and Gynæcology in Lisbon.

An international congress, organized by the Portuguese Society of Obstetrics and Gynæcology, will be held in Lisbon on September 19 and 20, 1959. The main subjects for discussion are: (i) present-day problems of diagnosis of uterine cancer; (ii) prevention of abortion; (iii) cœlioscopy in gynæcology (paper by Dr. R. Palmer, France).

This congress will be followed by the fourth congress of the International Union of Gynæcologists and Obstetricians, which will take place on September 21 and 22.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JUNE 13, 1959.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.[2]	Australian Capital Territory.	Australia.[2]
Acute Rheumatism	..	5	..	1	1	..	..	..	7
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	1	..	..	..	..	..	..	1
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	..	4(4)	..	..	..	..	..	..	4
Diphtheria	..	..	..	..	1(1)	..	..	..	1
Dysentery (Bacillary)	..	..	..	..	..	2	..	..	2
Encephalitis	..	..	..	..	..	..	..	..	..
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	1	..	..	1
Infective Hepatitis	64(22)	16(4)	13(4)	2	3	..	..	1	99
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	1	..	..	..	..	..	1
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	2	..	1	..	..	..	..	..	3
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	..	..	..	..	..	..	..	..
Puerperal Fever	1	..	2	..	..	..	..	..	3
Rubella	..	11(7)	..	..	1(1)	..	..	..	12
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	11(5)	13(9)	5	..	1(1)	..	..	1	31
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	36(12)	..	..	..	36
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	17(12)	13(5)	10(6)	12(10)	5(4)	2(2)	..	..	59
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

[2] Figures incomplete owing to absence of returns from Northern Territory.

The chief subjects for discussion are: (i) diagnosis of female genital cancer, from the economic and social points of view; (ii) criteria and methods of specialization in gynæcology and obstetrics; (iii) financial classification of obstetrical and gynæcological procedures from the economic or cost point of view.

There will be speakers from a number of countries, and a full social programme with many excursions is being arranged for members of the congresses and for their wives. The President is Professor Freitas Simoes (Lisbon) and the Secretary-General Dr. Mário Cardia (Porto). Inquiries should be directed to the Secretary-General at the following address: Dispensário Central de Higiene Social do Porto (Serviço de Ginecologia), Rua Anibal Cunha, 98, Porto, Portugal.

Australian Medical Board Proceedings.

NEW SOUTH WALES.

THE following additions and amendments have been made to the Register of Medical Practitioners for New South Wales, in accordance with the provisions of the *Medical Practitioners Act*, 1938-1958.

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (1) (a) of the Act: Compton, Ronald Murray, M.B., B.S., 1956 (Univ. Melbourne); Henderson, George Nicol, M.B., B.S., 1956 (Univ. Melbourne); Hodgson, Patricia Sophia, M.B., B.S., 1937 (Univ. Adelaide); James, Clive Henry Reynold, M.B., B.S., 1923 (Univ. Melbourne); Meehan, William Gerard, M.B., B.S., 1956 (Univ. Queensland); Tucker, Gaye Wayte, M.B., B.S., 1959 (Univ. Adelaide).

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (1) (b) of the Act: Brown, William Ashton Robert, M.B., B.S., 1955 (Univ. London); Campbell, John Gerrard, L., L.M., R.C.P. & S., (Ireland), 1949; Ellis, Angeline Elizabeth, M.B., B.Ch., 1939 (Univ. Witwatersrand); Eskdale, Sheila Mary, M.B., Ch.B., 1957 (Univ. Birmingham); James, Margaret, M.B., Ch.B., 1949 (Univ. Manchester); Kelly, Michael Joseph, L.A.H. (Dublin), 1950; Tan, Ngoh Chuan, M.B., B.S., 1955 (Univ. Malaya); Williams, Harold Bryan Lloyd, L.R.C.P. (London), 1943; Williams, David Bowen Morgan, M.B., B.Ch., 1953 (Univ. Wales), F.R.C.S. (England), 1957, B.Sc., 1950 (Univ. Wales).

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (2B) of the Act: Randmae, Georg, M.D., 1942 (Univ. Tartu); Szymiczek, Aloysius Nichols, M.D., 1934 (Univ. Budapest).

Medical Appointments.

Dr. R. J. J. Gray has been appointed Honorary Anæsthetist of the Royal Alexandra Hospital for Children, Camperdown, New South Wales.

Dr. R. P. Jepson has been appointed Honorary Surgeon at the Royal Adelaide Hospital, Adelaide.

Dr. H. N. Robson has been appointed Honorary Physician at the Queen Elizabeth Hospital, Adelaide.

Dr. A. D. Byrne has been appointed Honorary Gynæcologist at the Royal Adelaide Hospital, Adelaide.

Dr. G. W. E. Aitken has been appointed Honorary Assistant Gynæcologist at the Royal Adelaide Hospital, Adelaide.

Dr. R. M. Ford has been appointed Honorary Allergist at the Royal Adelaide Hospital, Adelaide.

Dr. D. A. Hicks has been appointed Honorary Assistant Physician in Charge of the Diabetic Clinic at the Royal Adelaide Hospital, Adelaide.

Dr. S. C. Milazzo has been appointed Honorary Visiting Medical Officer, Infectious Diseases Section (Northfield Wards), at the Royal Adelaide Hospital, Adelaide.

Dr. D. E. Dunn has been appointed Honorary Assistant Visiting Medical Officer, Infectious Diseases Section (Northfield Wards), at the Royal Adelaide Hospital, Adelaide.

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Langley, Alfred Robert McKenzie, M.B., B.S., 1958 (Univ. Sydney), "Thanet", 32 Warrangi Street, Turramurra.

Diary for the Month.

JULY 21.—New South Wales Branch, B.M.A.: Medical Politics Committee.
JULY 22.—Victorian Branch, B.M.A.: Branch Council.
JULY 23.—New South Wales Branch, B.M.A.: Clinical Meeting.
JULY 24.—Queensland Branch, B.M.A.: Council Meeting.
JULY 28.—New South Wales Branch, B.M.A.: Hospitals Committee.
JULY 30.—Western Australian Branch, B.M.A.: General Meeting.
JULY 30.—South Australian Branch, B.M.A.: Scientific Meeting.
JULY 30.—New South Wales Branch, B.M.A.: Branch Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales. Anti-Tuberculosis Association of New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference to an article in a journal the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

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